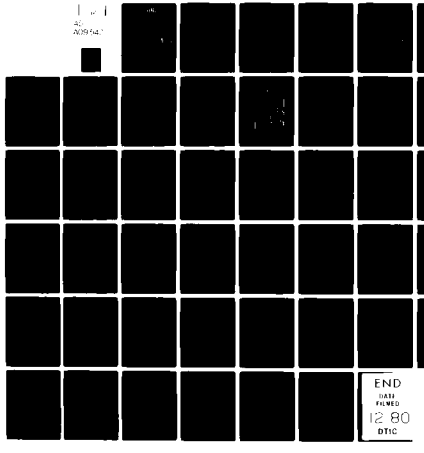
AD-A091 542 AIR FORCE INST OF TECH WRIGHT-PATTERSON AFB OH F/G 6/19
THE SINUSOIDAL RESPONSE OF THE OCULOVERSTIBULAR SYSTEM OF NORMA--ETC(U)
1979 B L GEORGE
UNCLASSIFIED AFIT-CI-79-180T NL



THE SINUSOIDAL RESPONSE OF THE OCULOVESTIBULAR SYSTEM OF NORMAL AND OTOLITH DEFICIENT MICE

A Thesis

Presented in Partial Fulfillment of the Requirements
for the Degree Master of Science

by

Bruce L. George, B.S., M.S.

The Ohio State University
1979

Approved by

Richard M. Cobbold
Adviser
Department of Electrical Engineering

UNCLASS

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

AFIT-CI-

REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

1. REPORT NUMBER: 79-180T	2. GOVT ACCESSION NO.: AD-A092 542
3. RECIPIENT'S CATALOG NUMBER	
4. TITLE (and Subtitle): The Sinusoidal Response of the Oculoverstibular System of Normal and Otolith Deficient Mice	5. TYPE OF REPORT & PERIOD COVERED: Thesis
	6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s): SSgt Bruce L. George	8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS: AFIT Student at: The Ohio State University	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
11. CONTROLLING OFFICE NAME AND ADDRESS: AFIT/NR, WPAFB OH 45433	12. REPORT DATE: Summer 1979
	13. NUMBER OF PAGES: 66
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)	15. SECURITY CLASS. (of this report): UNCLASS
	15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

Approved for public release; distribution unlimited

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

APPROVED FOR PUBLIC RELEASE AFR 190-17.

Fredric C. Lynch

FREDRIC C. LYNCH, Major, USAF
Director of Public Affairs

23 SEP 1980

18. SUPPLEMENTARY NOTES

Approved for public release; IAW AFR 190-17

Air Force Institute of Technology (ATC)
Wright-Patterson AFB, OH 45433

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Attached

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

UNCLASS

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

THESIS ABSTRACT

THE OHIO STATE UNIVERSITY
GRADUATE SCHOOL

The following information is to be submitted with the final copy of the thesis. Please type.

NAME BRUCE L. GEORGE Sgt. REGAF DEGREE M.Sc.

DEPARTMENT Electrical Engineering

TITLE OF THESIS The Sinusoidal Response of the Oculovestibular System of Normal and Otolith Deficient Mice

Summarize in the space below the purpose and principal conclusions of your thesis

The purpose of this research was to see if the otolith organs exert an influence upon horizontal semicircular canal induced nystagmus in response to horizontal angular acceleration. Both normal and otolith deficient mice were tested with sinusoidal inputs ranging from .02 hertz to 2 hertz.

The results showed a slight difference in the phase lags of the oculovestibular systems of the normal and otolith deficient mice. The normal mice had a slightly larger phase lag at corresponding frequencies than did the otolith deficient mice. This phase lag was greatest at low frequencies, approximately ten degrees.

It was concluded that the oculovestibular system in mice can be adequately compared to that system in man. That is, a second order transfer function for the semicircular canals and a lead-lag term for adaptation. It was also concluded that the otolith organs do influence semicircular canal induced nystagmus, possibly by modifying the adaptation time constant. This change in the adaptation time constant would produce results consistant with previously reported data which show a decrease in impulse induced nystagmus in otolith deficient mice.

Richard W. Smith
Adviser's Signature

(B)

Summer 1979
Quarter - Year

66 pages

Primary References

Hixson, W.C., Frequency response of the oculovestibular system during yaw oscillation. NAMRL-1212. Pensacola, Florida, 1974.

Malcolm, R. and Melvill-Jones, G., A quantitative study of vestibular adaptation in humans. Acta Otolaryng. (Stockh.), 70: 126-135, 1970.

ACKNOWLEDGEMENTS

I wish to thank John Wyrick, the undergraduate research assistant who assisted me in the performance of the experiments, and Phil Fisher and Renee Figgs for their aid in data reduction. I would especially like to thank Dr. Richard Campbell and Dr. David Clark for their strength and guidance throughout the research and preparation of this thesis. Finally, I would like to thank my wife, Joan, for her support and understanding during my entire period of study.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

INTRODUCTION

During the last two decades, extensive research has been conducted on the vestibular apparatus. This research has centered upon the two main organs of equilibrium, the semicircular canals and the otolith organs. Specifically, most research has attempted to detail and model the function of these two sensory organs.

Recently, it has been suggested that these two independent sensory systems may interact to produce the animal's overall response to stimulation. The purpose of this research was to attempt to define this interaction between the otolith organs and the semicircular canals. Specifically, its purpose was to see if the otolith organs exerted an influence on semicircular canal induced nystagmus in response to horizontal angular acceleration. For this experiment, a genetic strain of mice (pallid) were used that anatomically had varying degrees of otolith deficiency, ranging from near normal otolith development to almost no otolith development. Using both sinusoidal and impulse inputs of acceleration, the oculovestibular systems of ten pallid mice were examined. From the results obtained, it appears that the otoliths do indeed have an influence upon the semicircular canal induced nystagmus.

The general anatomy and physiology of these two sensory structures was well documented by 1960. Groen (1956-1957) presents a good review of these features, as follows. The otolith organs (Figure 1) consist of otolithic crystals imbedded in a jelly-like layer which rests upon a macula (a layer of both supportive and sensory cells) and within a sac-like enclosure of the labyrinth (the sacule or utricule). The otolith is supported so as to allow a sliding movement above the macula. Sensory cell cilia extend from the macula through a jelly-like interface to the otolith. Movement of the otolith thus causes tension and movement of these cilia, which in turn translate the mechanical stimulation into a neural response. This anatomical configuration makes the otolith organs receptors of linear acceleration and its direction. The semicircular canals consist of three orthogonal loops of bone, each with an enlarged area, the ampula (Figure 2). Within the ampula, a basal collection of sensory and supportive cells (the crista), send sensory cell cilia into a jelly-like structure, the cupula. Motion of the cupula causes motion of the cilia and as in the otolith organs, this mechanical stimulation is translated into the neural message. The bending of the cupula is accomplished by the inertial forces of the fluid that fills the semicircular canals. Here the anatomical configuration yields receptors sensitive to angular acceleration.

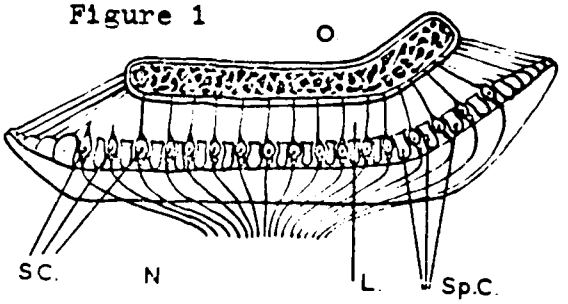
In both the otolith organs and the semicircular canals, the neural message appears to be encoded in the frequency of firing of neural impulses. In the otolith organs, as the otolith changes position, it causes an increase in the firing rate of selected sensory

cells. Similarly, in the semicircular canals, the deflection of the cupula seems to determine the firing rate of the crista's sensory cells.

Since the time of Groen's review, this classical representation of two independent sensory organs, one a receptor of linear acceleration and one a receptor of angular acceleration, has been modified. It now appears that these two systems, while probably responding to different stimuli, are not independent in their action. Studies on humans rotated in a centrifuge, indicate that the otoliths exert a modifying effect upon the output of the semicircular canals (Lansberg, 1965). Studies on mice, genetically deficient in their otolith organ development, also point to an effect on the semicircular canals by the otolith organ (Coccia, 1975).

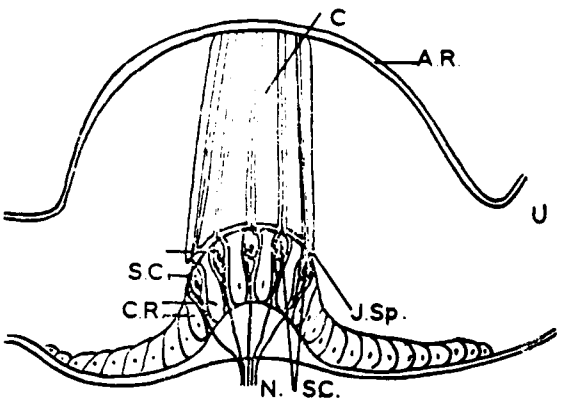
This research tended to support this idea, that the otolith organs do interact with the semicircular canals.

Figure 1



Schematic drawing of a cross section of an otolith and its macula. O. is the otolith, suspended by strands which run from the margins to the macula consisting of supporting cells (Sp.c.) and sensory cells S.C. Between the otolith and the macula there is a thin layer (L.) to allow the otolith to slide over the macula. N. is the nerve.

Figure 2



Schematic drawing of a cross section through an ampulla, with cupula and crista. A.R., ampulla roof. C.R., crista, consisting of S.C. (sensory cells), supporting cells and N. (nerve fibres). Between cupula and crista there is the I.S.P. (intercupular space). U., utricule.

(Reprinted from Groen, 1956-1957)

METHODS AND MATERIALS

Nystagmus

Semicircular canal function is usually examined by one of two means, direct recording from the associated neurons or nystagmography. The former is the more direct method and would give data isolated from any otolith influence (which presumably would be at higher level neurons in the central nervous system). The latter is more direct and represents the end result of all signal processing.

Nystagmus can be defined as smooth pursuit movements alternated with rapid repositioning saccadic jumps (Jones, 1973). The function of nystagmus may be defined as the stabilization of the field of view during motion (Jones, 1973). That is, for the purpose of equilibrium, when the head is turned in one direction, the eyes remain fixed on a stationary point and thus rotate in the opposite direction of the head but at the same speed. After the head has moved through a specified distance, the eyes return rapdily in the direction of head motion to a new fixation point and begin their slow motion pursuit again.

Mathematical Relationship of Nystagmus to the Semicircular Canals

Classically, the semicircular canal has been mathematically defined as a torsion pendulum with the following differential equation relating the cupula to angular acceleration of the head (Groen, 1956-1957 and Hixson, 1974).

$$\ddot{\theta}_c + \frac{\Pi}{I}\,\dot{\theta}_c + \frac{\Delta}{I}\,\theta_c = \theta_H \tag{1}$$

$\ddot{\theta}_c$, $\dot{\theta}_c$, θ_c = Angular acceleration, velocity and displacement of cupula

θ = Angular acceleration of head

Π = Damping coefficient

I = Moment of inertia of fluid ring

Δ = Stiffness coefficient

Rearranged and represented by Laplace rotation, this equation becomes:

$$\frac{\theta_c}{\theta_H} = \frac{1}{(S + W_1)\,(S + W_2)} = \frac{K}{(T_1 S + 1)\,(T_2 S + 1)} \tag{2}$$

W_1, W_2 = Lower and upper corner frequencies of the cupula

T_1, T_2 = Long and short time constants of the cupula

$K = T_1 T_2$

$$T_1 = \frac{\Pi}{\Delta} = \frac{1}{W_1}$$

$$T_2 = \frac{I}{\Pi} = \frac{1}{W_2}$$

If one now assumes that the eyes undergo nystagmus due to cupular deflection (Groen, 1956-1957), then nystagmus (specifically the slow phase velocity component) can be related to angular acceleration of the head by equation 2. Thus nystagmus would increase with increased angular acceleration and disappear when the angular acceleration is zero.

Recent studies have suggested that nystagmus is not directly related to cupular deflection but to the difference between cupular deflection and a shifting reference level (Young and Oman, 1969 and Malcolm and Jones, 1970). This shifting reference level is believed to be an adaptation mechanism in the central nervous system and can be represented by the following transfer function (Young and Oman, 1969):

$$\frac{\Theta_e}{\Theta_c} = \frac{S}{S + 1/T_a}$$

Θ_e = Angular slow phase nystagmus velocity

Θ_c = Angle of cupular deflection

T_a = Adaptation time constant

Combining this adaptation factor with the mechanics of the semicircular canal gives the following overall transfer function:

$$\frac{\Theta_e}{\Theta_H} = \frac{KS}{(T_1S + 1)\ (T_2S + 1)\ (T_aS + 1)}$$

K = An overall gain constant

Thus the slow phase nystagmus angular velocity is now directly related to the angular acceleration of the head.

Procedure

In an attempt to better define the interaction between the otolith organs and the semicircular canals, sinusoidal analysis of the oculovestibular system was carried out on ten pallid mice. Pallid mice are a genetic strain of the common mouse (Mus musculus) that have varying degrees of deficiency in their otolith development. Their semicircular canal development, however, appears normal. This makes the pallid mice ideally suited for examination of otolith-canal interaction.

Each mouse was initially sedated for placement in the test device (Figure 3). The mouse was positioned with head and body immobilized on a rate table so that the horizontal canals would be in the plane of motion of the table. The rate table was manufactured by Inland Control (Model 823) and provided accurate motion for both internally generated steps of velocity and externally driven sinusoidal velocities. Tachometer feedback from the table was compared to input stimulation for accuracy of motion to .1% of selected rate or .01% of full scale of selected range, whichever is greater.

Grass E2B subdermal electrodes were inserted into the inner and outer canthus of the eye, for corneo-retinal recording of the nystagmus (Groen, 1956-1957). A third electrode was placed in the ear of the mouse as a common ground for differential recording. The electrodes were then connected through the slip rings of the rate table to a

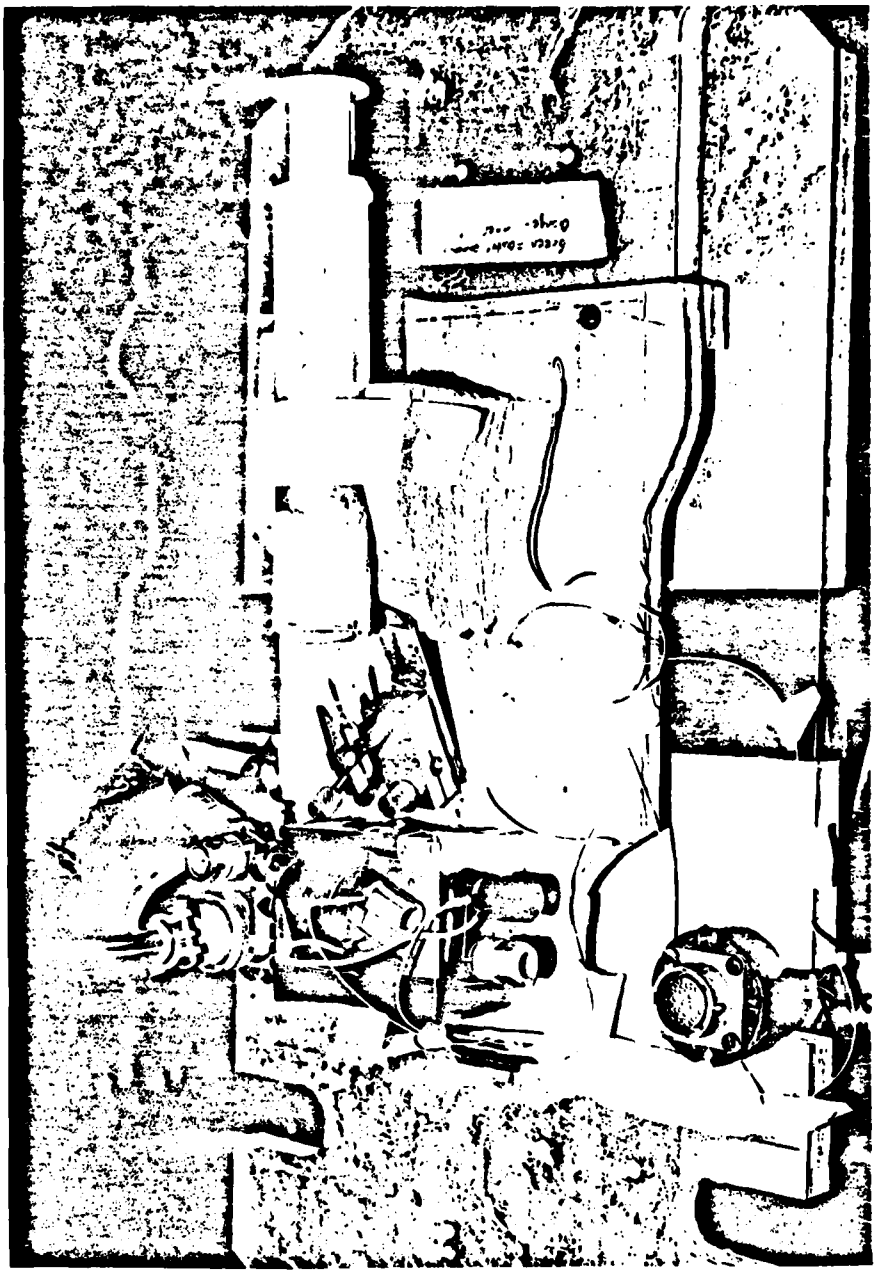


Figure 3. Rate Table and Mouse Restraint

Grass P16 high input impedence AC amplifier for initial gain and stabilization of the signal. The signal was then sent through a Grass 7P3A AC preamplifier and DC Driver amplifier for chart recording. The frequency characteristics of the amplifiers (Figure 4) were selected to yield the best possible recording of the nystagmus.

A Krohn-Hite (Model 5100-A) function generator was used for sinusoidal velocity input drive to the rate table, calibrated through the rate table control to provide a constant maximum velocity for all frequencies of stimulation.

At times a Grass P16 AC/DC amplifier and Grass 7P1A DC preamplifier were used to obtain DC recordings and at other times a Grass differentiator was used to provide the third trace on the chart. In all recordings the nystagmus (AC recording) and the velocity of the table (Tach output) were traced on the chart.

Primarily sinusoidal stimulation was used but steps of velocity of 250°/sec and 350°/sec were also used. The sinusoidal stimulation ranged from .02Hz to 1Hz. Recordings, however, from the lower frequencies and highest frequencies were often impossible to interpret.

Due to the difficulty in calibrating eye movement with recording, only phase characteristics of the nystagmus were examined for the sinusoidal stimulation. Phase measurements were made as in Figure 5 following the procedure outlined by Hixson (1974).

The mice were allowed a recovery time (15-30 minutes) before recordings were taken and a warm up time at each frequency, usually amounting to a few cycles, before data measurements were taken, to yield steady state responses at each frequency.

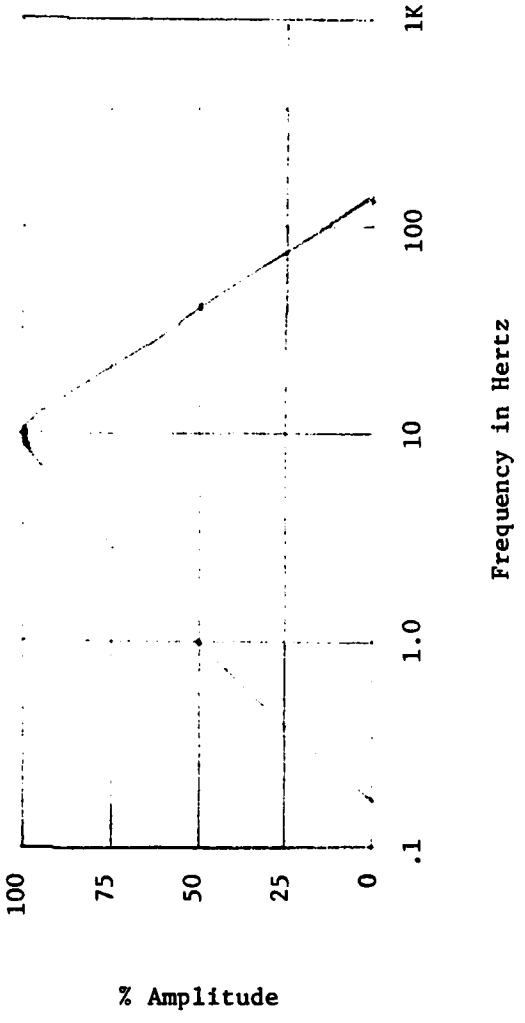


Figure 4. Frequency Response of Amplifiers

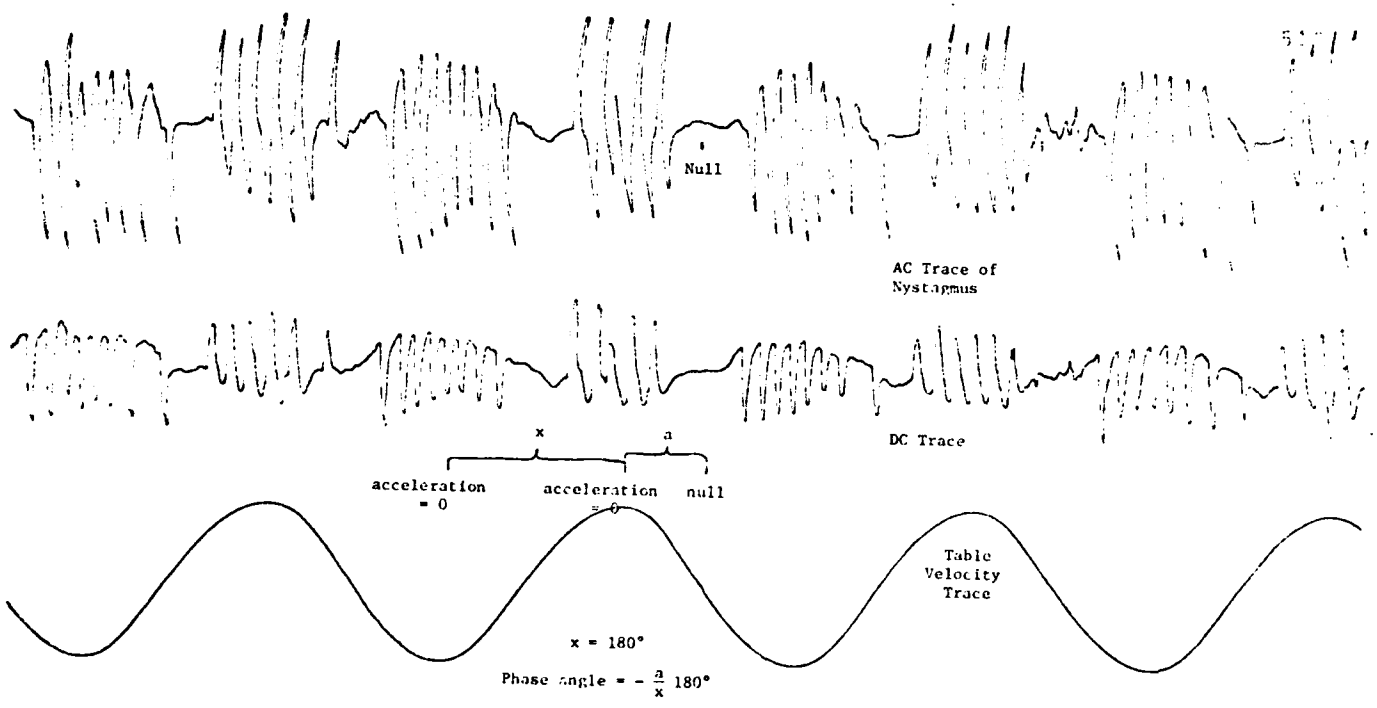


Figure 5. Measurement of Nystagmus Phase Angle

RESULTS

The phase lags for ten pallid mice are shown in tables one through ten. For each mouse, the frequency of stimulation, the mean phase lag, the standard deviation and the direction of motion are given. The frequencies of stimulation ranged from .04Hz to 1Hz with measurements taken only when the mouse showed reasonable response. An attempt was made to measure at least ten phase angles in each direction of motion at each frequency, for the determination of the mean phase lag and standard deviation. However, it was not always possible to measure this many angles due to a mouse's inconsistancy of response. The direction of motion is taken as clockwise when the response null followed a peak of velocity in the clockwise direction, and as counterclockwise when the response null followed a peak of velocity in the counterclockwise direction. Phase Bode plots for the ten mice are shown in Figures 6 through 25.

Examination of the tabular data and phase plots reveal the inconsistancy of the phase angles. There was often wide variations in phase angle for a particular frequency for an individual mouse. This is demonstrated by the often large standard deviations around the mean phase angles. In general the best recordings of nystagmus

occurred between the frequencies of .06Hz to .2Hz. Measurements outside this range were often taken from poor nystagmus recordings and therefore conclusions drawn were not based upon those measurements.

Of the ten pallid mice, seven are near normal in their otolith development and three are nearly totally deficient in their otolith development. This categorizing of the mice are based upon swimming tests done on the mice by Dr. D.J. Lim of The Ohio State University. In this test the mice are classified as being normal swimmers, vertical swimmers or underwater circular swimmers. The normal swimmers have been shown to be near normal in their otolith development while the underwater circular swimmers are nearly totally deficient in their otolith development and the vertical swimmers show intermediate deficiency in their otolith development.

Summarized results of the seven normal swimmers are given in table 11 and a phase bode plot for these mice is shown in Figures 26 and 27. Summarized results of the three underwater circular swimmers are given in table 12 and a phase bode plot for these mice is shown in Figures 28 and 29.

Examination of the phase bode plots in Figures 27 and 29 reveal a slight shifting upward of the bode plot for the underwater circulars. That is there appears to be slightly less phase lag (near 10° at low frequencies) in the underwater circulars.

DISCUSSION

Data Collection

There are numerous difficulties associated with measuring nystagmus. Stockwell and Collins (1973) discuss three areas where practical problems occur. The first of these is the actual recording of the nystagmus. We chose to place electrodes in the inner and outer canthus of the eye with slight outward pressure to obtain the best electrical contact. This method of electrode attachment, however, yielded approximately 70K ohms of resistance between the electrodes (as measured by a Simpson meter). Stockwell and Collins (1973), however, feel there should be less than 10K ohms impedence between electrodes for best recording. It is not known if this higher impedence introduced any added problems in our recording.

Both AC and DC recording of the nystagmus was attempted, but the problem of DC drift often made DC recording too difficult. Therefore, for the ten pallid mice studied, only AC recording was utilized. This means that accurate eye position observation was impossible as only DC recording can accurately measure eye position (Stockwell and Collins, 1973). For AC recording, Stockwell and Collins (1973) suggest a bandwidth from .053Hz to 30Hz to give the best fidelity. However, due

to noise problems, we found our best recordings were made with a bandwidth from 1Hz to 35Hz. Thus, this shifting of the bandwidth might mean a degradation of the fidelity of the recording.

A second major source of possible error is the recording of other electrical events by the electrodes (Stockwell and Collins, 1973). Often it is difficult to distinguish potential changes due to muscle movements of the face and potentials due to blinking from those of nystagmus. These other potentials also may mask underlying nystagmus potentials so that determination of onset or cessation of nystagmus is not always clear.

Lastly it is known that in man, nystagmus is suppressed during relaxed periods (Stockwell and Collins, 1973). Often subjects are asked to do mental exercises to keep a state of alertness necessary for good nystagmus recordings. In these experiments, since the mouse was anesthetized for electrode insertion, there exists a possibility that the mouse might have suffered a lingering effect of the anesthetic. Thus, the state of alertness of the mice was an unknown that also could have influenced our nystagmus recordings.

In summary, these three problem areas, the instrumentation and technique, the presence of other potentials and the alertness of the mice, may have introduced some error into the accurate determination of the null point of nystagmus. It is this error that could account for the wide variation he phase lag angles measured on this group of ten mice. The average standard deviation for the summarized results of 9.8° is certainly higher than a mean standard deviation of 4.7° seen in the response of human subjects tested by Hixson (1974).

The Oculovestibular System of Mice

It appears safe to assume that the oculovestibular system of the mouse is similar to that found in man. Precht (1979) states that similar neural connections are found in the oculovestibular systems of the frog, cat and rabbit. These connections include both direct (3 neuron pathway) and indirect (through the central nervous system) pathways in these three species (Precht, 1979). Thus, we can reasonably assume that a transfer function similar to that for man can be applied to the mouse. That is a second order system for the response of the semicircular canal and a lead-lag term for adaptation. The canal term being derived from the mechanics of the system and the adaptation term arising somewhere in the indirect pathway through the higher centers of the brain.

By the method of visual curve fitting, rough estimates of the time constants for the oculovestibular system of the normal swimming mice yield .1 and 4 second time constants for the canal themselves and 32 seconds for the adaptation time constant (Figure 30). This corresponds to corner frequencies of 1.5Hz, .04Hz and .005Hz. Thus the transfer function of the oculovestibular system can be represented by the following equation:

$$\frac{\Theta_e}{\Theta_H} = \frac{KS}{(.1S + 1)\ (4S + 1)\ (32S + 1)}$$

$T_1 = .1$ sec $\quad T_2 = 4$ sec $\quad T_a = 32$ sec

The Interaction Between the Semicircular Canals and the Otoliths

Precht (1979) gives good neurological evidence for a possible interaction between the semicircular canals and the otolith organs. He mentions strong canal-otolithic convergence in the oculovestibular pathways more so for vertical and oblique eye muscles but also for the horizontal system. Furthermore, he points out that many of the secondary vestibular fibers that terminate at the motor nuclei controlling eye movement already contain both canal and otlith signals. Also, Coccia (1975) in her dissertation gives good behavioral evidence for a possible interaction as she found evidence that the otolith organs produced an affect upon canal induced nystagmus. Her results showed that a deficiency of otolith stones in the otolith organs caused a shortening of the duration of nystagmus following an impulse of acceleration.

If one compares the phase bode plots for the normal and underwater circular swimmers, we see a small but maybe not statistically significant shift of the curve upward in the underwater circulars. If one assumes that the time constants for the mechanics of the semicircular canals exhibits the same influence on the curve in both groups of mice, then one can modify only the adaptation time constant to yield the noted change in the curve. Again using a visual method for best fit, the curve for underwater circular swimmers yields an adaptation time constant around 11 seconds (Figure 31). Thus the transfer function for the oculovestibular system in the underwater circular swimmers could be represented by the following approximate

transfer function.

$$\frac{\Theta_c}{\Theta_H} = \frac{KS}{(.1S + 1)\ (4S + 1)\ (11S + 1)}$$

Since adaptation takes place in the higher levels of the indirect pathways, it may be reasonable to assume that otolith influence may also be found in these levels. Thus it may not be unreasonable to believe that the otoliths interact with the adaptation mechanism of the semicircular canals.

Since an impulse of acceleration will be due largely to the long time constant of adaptation, alteration of this time constant would alter the duration of nystagmus. Thus, if the lack of otolith development, and hence influence, decreases the adaptation time constant, we would expect a shortening of the nystagmus response to an impulse of acceleration.

Referring to Malcolm's (1970) discussion of the adaptation mechanism based upon a shifting reference level, the rate of change of the reference level can be expressed by the following equation:

$$\frac{dR}{dt} = b\ (\Theta_c - R)$$

Θ_c = cupula deflection

R = reference level

In Laplace notation this equation becomes:

$$\frac{R}{\Theta_c} = \frac{b}{S + b} = \frac{1}{T_a S + 1} \qquad \text{where } T_a = \frac{1}{b}$$

Thus a decrease in T_a would mean an increase in b and a faster rate of change of the reference level. Since the reference level is continuously changing to decrease the difference between cupular deflection and itself, a faster rate of change would mean a shortening of both the primary and secondary nystagmus.

This agrees with Coccia's (1975) results on tilted head mice.

Before continuing with the idea that the otolith influence is upon the adaptation time constant, it must be mentioned that other hypothesis could be put forward to explain the results of the experiment.

For example, if we allow for a more complicated signal processing by the central nervous system (certainly possible), then the output nystagmus response may not yield accurate measurements of the semicircular canal constants. Instead, the output may be a complicated sum of inputs from many sources, canals, otoliths, proprioceptive and visual. It has been postulated that the semicircular canals respond best at higher frequencies and the otolith organs best at low frequencies. Since the results show the greatest curve difference between normal and otolith deficient mice at low frequencies, this difference could be explained by the loss of low frequency data (presumably from the otoliths) in the otolith deficient mice.

The results also could be explained by a frequency dependant threshold sensor that relies upon otolith input. Its presumed function would be to limit response to inputs beyond a minimum cupular deflection. If it was related to otolith input and introduced some phase lag into the overall system, its alteration in the otolith deficient

mice might both decrease the phase lag as noticed in this experiment and shorten the duration of nystagmus by raising the threshold level.

An attempt can now be made to put together some of our information about the oculovestibular system into a theoretical model (Figure 30). Our inputs would consist of angular acceleration to the semicircular canals and the linear component of angular acceleration to the otolith organs. It can then be assumed that there are direct lines to the eye muscles from both receptors and indirect lines through the central nervous system to the eye. The output will be assumed to be the slow phase velocity of nystagmus and the central nervous system will be assumed to contain a neural integrator to convert cupular deflection and otolith organ output into velocity measurements. Proprioceptive feedback from the eye muscles was included but any time delays, threshold sensors and terms for eye muscle dynamics were not. Also visual feedback is not included as this pathway was eliminated during the experiment.

This simple model does not take into account all the complexities of the system especially at the level of the control nervous system. It does not include all the various pathways identified by Precht (1979) or the multitude of interactions that take place in the central nervous system. It does, however, suggest a possible site of action for the otolith input, that is in the adaptation of the oculovestibular system to angular acceleration.

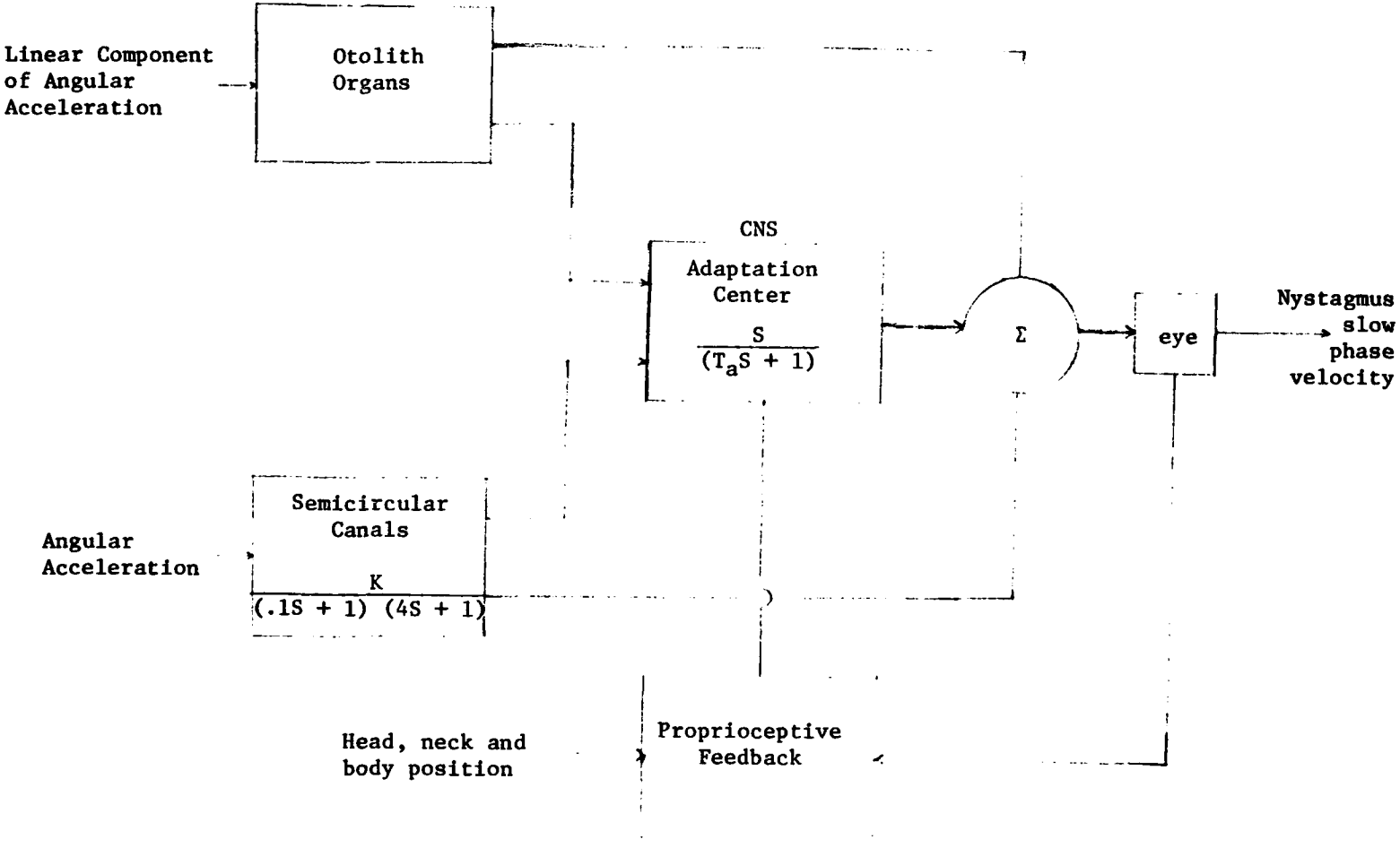

Linear Component of Angular Acceleration
Otolith Organs
CNS
Adaptation Center
S / (TaS + 1)
Σ
eye
Nystagmus slow phase velocity
Angular Acceleration
Semicircular Canals
K / (.1S + 1) (4S + 1)
Head, neck and body position
Proprioceptive Feedback

Figure 30

Directional Differences of Nystagmus

Examination of the results indicates slight differences in the phase angles measured for the two different directions of motion, clockwise and counterclockwise. Also examination of the nystagmus recordings often revealed differences in the length, amplitude and quality of the nystagmus for the two directions of motion.

A possible explanation for this could be that the coupling between the left and right oculovestibular systems in mice is not as complete as in man. Hence the left eye and left semicircular canal might dominate for motion in one direction and the right eye and right semicircular canal might dominate for motion in the opposite direction. Specifically, the left oculovestibular system might dominate in counterclockwise motion and the right might dominate in clockwise motion.

However, for whatever reason the phase angle measurements differ, the final analysis of system was done using primarily the counterclockwise data from left eye recordings.

Areas of Future Research

Initially more work needs to be done with the pallid mice. More extensive experimentation of their sinusoidal and impulse responses need to be carried out. Time did not permit analysis of the impulse responses obtained to see if they agree with expected results, and the number of mice examined is insufficient for good statistical analysis.

More work also needs to be done in the neurological area, coordinating the pathways found with function. Expanding the model of the central nervous system is of the utmost importance in understanding the interaction of the otolith organs and the semicircular canals.

SUMMARY

The sinusoidal response of the oculovestibular system of pallid mice yielded the following conclusions.

1) The oculovestibular system of mice can be adequately compared to that system in man. That is, a second order transfer function for the semicircular canals and a lead-lag adaptation term with the approximate mathematical representation of:

$$\frac{\Theta_e}{\Theta_H} = \frac{KS}{(.1S + 1)\ (4S + 1)\ (32S + 1)}$$

Θ_e = Nystagmus slow phase velocity

Θ_H = Head angular acceleration

2) The otolith organs would influence the semicircular canal induced nystagmus by increasing the duration of postrotary nystagmus.

3) The effect of the otolith organs could be explained by a modification of the short term adaptation of the semicircular canal induced nystagmus.

4) The oculovestibular system for otolith deficient mice can be represented by the following approximate transfer function:

$$\frac{\Theta_e}{\Theta_H} = \frac{KS}{(.1S + 1)\ (4S + 1)\ (11S + 1)}$$

Table I

Mouse #15 Left Eye

Clockwise Motion

Frequency in Hz	Mean Phase Angle in Degrees	Standard Deviation in Degrees
.03	-44	4
.05	-28	11
.06*	-41	7
.07	-37	8
.08	-49	15
.09	-55	17
.1	-51	13
.125	-58	4
.15	-64	13
.175	-69	6
.2	-88	16
.225	-87	6
.3	-101	6
.45	-86	6
.5	-96	7
.6*	-101	--
.7	-94	3
.8*	-84	7
.9	-106	10
1.0	-101	13
1.5	-102	10
2.0	-126	6

*Results from measurements taken on right eye

Table I (Cont.)

Counterclockwise Motion

Frequency in Hz	Mean Phase Angle in Degrees	Standard Deviation in Degrees
.04	-35	11
.05	-29	11
.06*	-51	5
.07	-67	14
.08	-48	8
.09	-55	9
.1	-54	15
.125	-71	12
.15	-73	37
.175	-98	8
.225	-92	17
.25	-98	11
.3	-97	6
.45	-120	9
.5	-113	4
.7	-107	8
.9	-115	11
1.0	-104	--
1.5	-98	3
2.0	-126	5

*Results from measurements taken on right eye

Table II

Mouse #10 Left Eye

Clockwise Motion

Frequency in Hz	Mean Phase Angle in Degrees	Standard Deviation in Degrees
.04	-37	3
.06	-43	14
.07	-56	14
.08	-57	12
.1	-57	10
.15	-58	7
.2	-67	6
.3	-89	5
.4	-104	7
.5	-92	3
.6	-93	6
.8	-112	15

Counterclockwise Motion

.04	-25	33
.06	-47	8
.07	-34	10
.08	-43	13
.1	-60	7
.3	-94	4
.4	-107	6
.5	-96	4
.6	-109	6
.8	-112	5

Table III

Mouse #12 Left Eye

Clockwise Motion

Frequency in Hz	Mean Phase Angle in Degrees	Standard Deviation in Degrees
.04	-39	15
.05	-50	12
.06	-58	3
.07	-69	16
.08	-68	10
.09	-82	8
.1	-81	8
.125	-87	6
.15	-97	6
.175	-98	5
.2	-100	5
.25	-106	3
.4	-110	6
.5	-121	8
.6	-106	5

Counterclockwise Motion

.04	-39	14
.05	-49	15
.06	-57	6
.07	-46	11
.08	-54	7
.09	-46	4
.1	-69	4
.125	-84	12
.15	-82	6
.175	-85	5
.2	-85	9
.25	-85	4
.4	-100	3
.5	-101	4
.6	-112	7

Table IV

Mouse #4 Left Eye

Clockwise Motion

Frequency in Hz	Mean Phase Angle in Degrees	Standard Deviation in Degrees
.03	-36	10
.04	-47	4
.05	-54	6
.06	-53	12
.07	-57	7
.08	-78	7
.09	-69	8
.1	-71	13
.125	-77	9
.15	-98	7
.175	-77	9
.2	-79	4
.25	-85	4
.4	-84	8
.6	-99	7
.7	-100	3

Counterclockwise Motion

.03	-25	10
.04	-48	7
.05	-58	4
.06	-63	9
.07	-63	2
.08	-64	9
.09	-72	7
.1	-77	6
.125	-75	7
.15	-86	4
.175	-92	6
.2	-109	12
.25	-95	6
.4	-109	15
.6	-103	11
.7	-104	2

Table V

Mouse #13 Left Eye

Clockwise Motion

Frequency in Hz	Mean Phase Angle in Degrees	Standard Deviation in Degrees
.02	-44	22
.04	-47	5
.05	-41	17
.06	-40	7
.07	-47	10
.08	-37	4
.09	-64	10
.1	-69	6
.125	-72	9
.15	-77	17
.175	-84	7
.2	-95	5
.25	-91	4
.4	-98	3
.6	-103	6

Counterclockwise Motion

.02	-55	19
.04	-51	6
.05	-38	--
.06	-65	3
.07	-68	14
.08	-56	21
.09	-68	6
.1	-73	15
.125	-85	7
.15	-70	13
.175	-85	10
.2	-83	7
.25	-94	7
.4	-100	5
.6	-102	8

Table VI

Mouse #19 Left Eye

Clockwise Motion

Frequency in Hz	Mean Phase Angle in Degrees	Standard Deviation in Degrees
.04	-27	5
.06	-35	11
.07	-47	10
.08	-68	14
.09	-55	10
.1	-88	--
.125	-64	14
.15	-102	7
.175	-92	10
.2	-88	24
.25	-79	13
.4	-92	13
.6	-97	15
.7	-95	13

Counterclockwise Motion

.04	-28	14
.06	-43	13
.07	-48	10
.08	-47	7
.09	-74	11
.1	-56	6
.125	-81	14
.15	-71	5
.175	-82	11
.2	-81	7
.25	-96	6
.4	-97	7
.6	-99	7
.7	-95	13

Table VII

Mouse #18 Left Eye

Clockwise Motion

Frequency in Hz	Mean Phase Angle in Degrees	Standard Deviation in Degrees
.03	-23	16
.04	-15	7
.05	-29	10
.06	-33	4
.07	-44	7
.08	-41	12
.09	-44	5
.1	-44	5
.125	-56	10
.15	-55	8
.175	-63	14
.2	-63	5
.25	-61	3
.4	-75	6
.6	-96	3

Counterclockwise Motion

.03	-35	12
.04	-44	11
.05	-53	17
.06	-59	13
.07	-70	10
.08	-67	11
.09	-71	4
.1	-84	7
.125	-82	2
.15	-95	6
.175	-97	16
.2	-104	4
.25	-111	13
.4	-84	3
.6	-123	7

Table VIII

Mouse #3 Left Eye

Clockwise Motion

Frequency in Hz	Mean Phase Angle in Degrees	Standard Deviation in Degrees
.05	-52	4
.06	-36	8
.07	-45	11
.08	-49	6
.09	-51	8
.1	-53	8
.125	-67	8
.15	-50	16
.175	-66	18
.2	-70	13
.25	-86	5
.4	-102	6
.6	-112	9
.7	-111	5

Counterclockwise Motion

.05	-32	--
.06	-39	7
.07	-44	7
.08	-57	10
.09	-50	6
.1	-64	5
.125	-67	7
.15	-76	14
.175	-75	11
.2	-90	12
.25	-87	4
.4	-88	9
.6	-96	10
.7	-97	8

Table IX

Mouse #11 Left Eye

Clockwise Motion

Frequency in Hz	Mean Phase Angle in Degrees	Standard Deviation in Degrees
.06	-29	6
.07	-40	13
.08	-49	7
.09	-48	--
.1	-55	5
.125	-84	4
.15	-83	5
.175	-100	--
.2	-91	6
.4	-97	12
.6	-90	12
.7	-67	11

Counterclockwise Motion

.06	-45	8
.07	-54	7
.08	-46	4
.09	-68	8
.1	-52	5
.125	-68	6
.15	-62	9
.175	-82	7
.2	-73	9
.4	-93	7
.6	-101	6
.7	-72	7

Table X

Mouse #17 Left Eye

Clockwise Motion

Frequency in Hz	Mean Phase Angle in Degrees	Standard Deviation in Degrees
.04	-39	11
.05	-47	12
.06	-48	18
.07	-54	14
.08	-38	4
.09	-46	6
.1	-42	4
.125	-59	8
.15	-50	5
.175	-71	11
.2	-64	11
.25	-83	16
.4	-98	11
.6	-107	15
.7	-106	--
.9	-119	4

Counterclockwise Motion

.04	-33	11
.05	-37	12
.06	-50	18
.07	-47	13
.08	-42	3
.09	-49	7
.1	-53	4
.125	-71	15
.15	-80	1
.175	-87	5
.2	-92	10
.25	-94	7
.4	-84	5
.6	-95	5
.7	-101	6
.9	-103	9

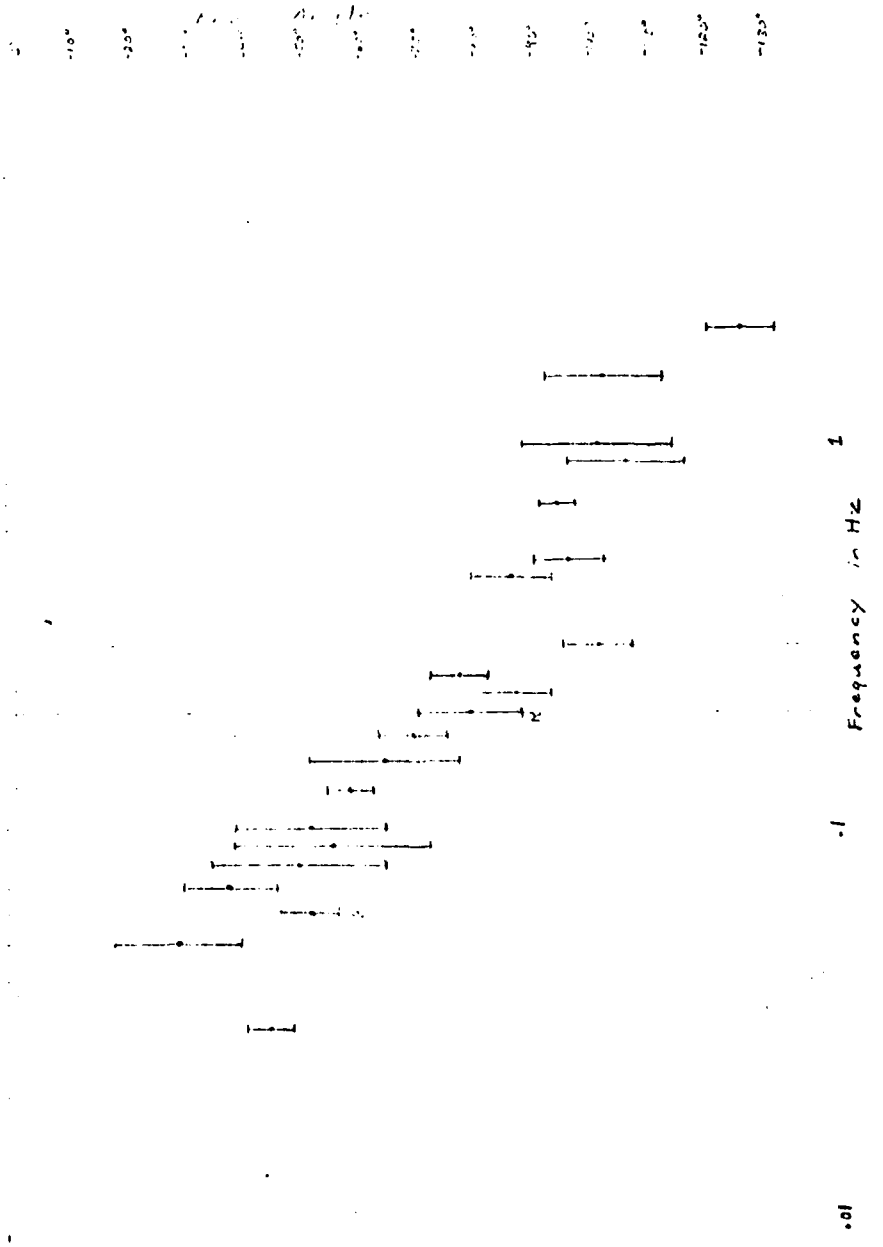


Figure 6. Phase Bode Plot of Mouse #15
Left eye, clockwise data
Right eye, counterclockwise data

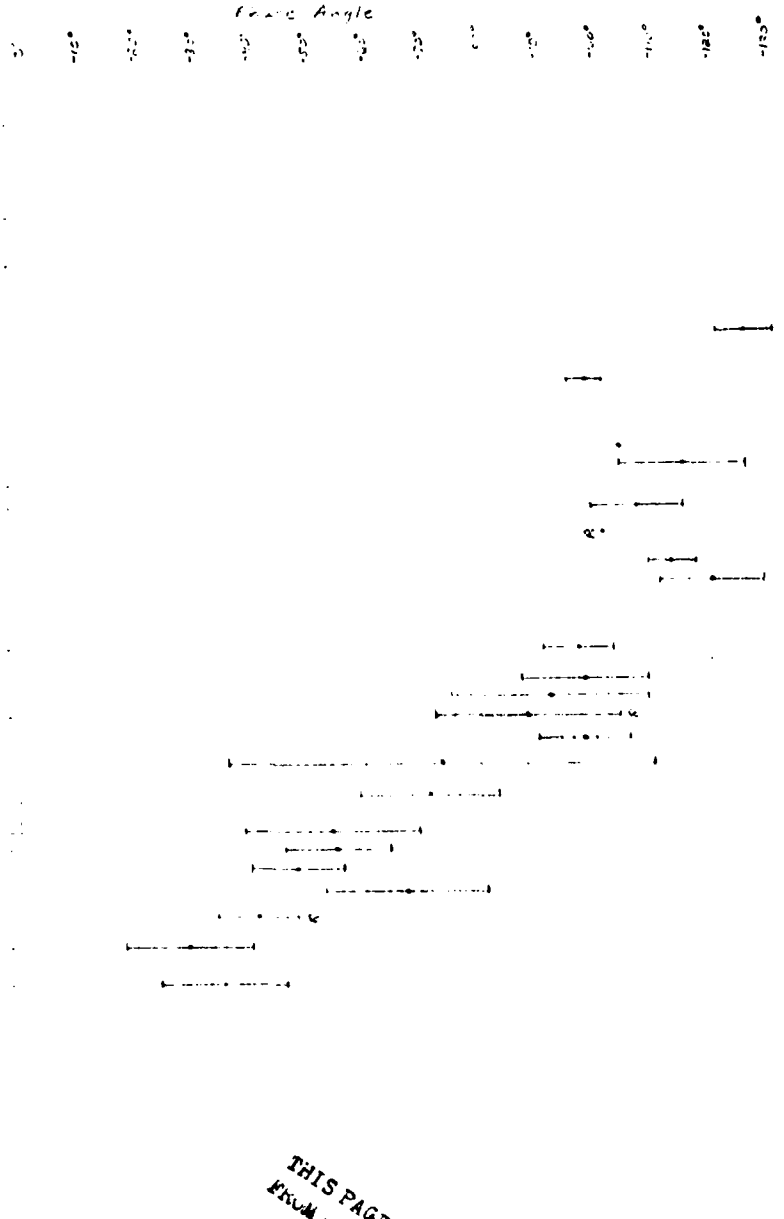


Figure 7. Phase Bode Plot of Mouse #15
Left eye, counterclockwise data
Right eye, clockwise data

Figure 8. Phase Bode Plot of Mouse #10
Left eye, clockwise data

Figure 9. Phase Bode Plot of Mouse #10
Left eye, counterclockwise data

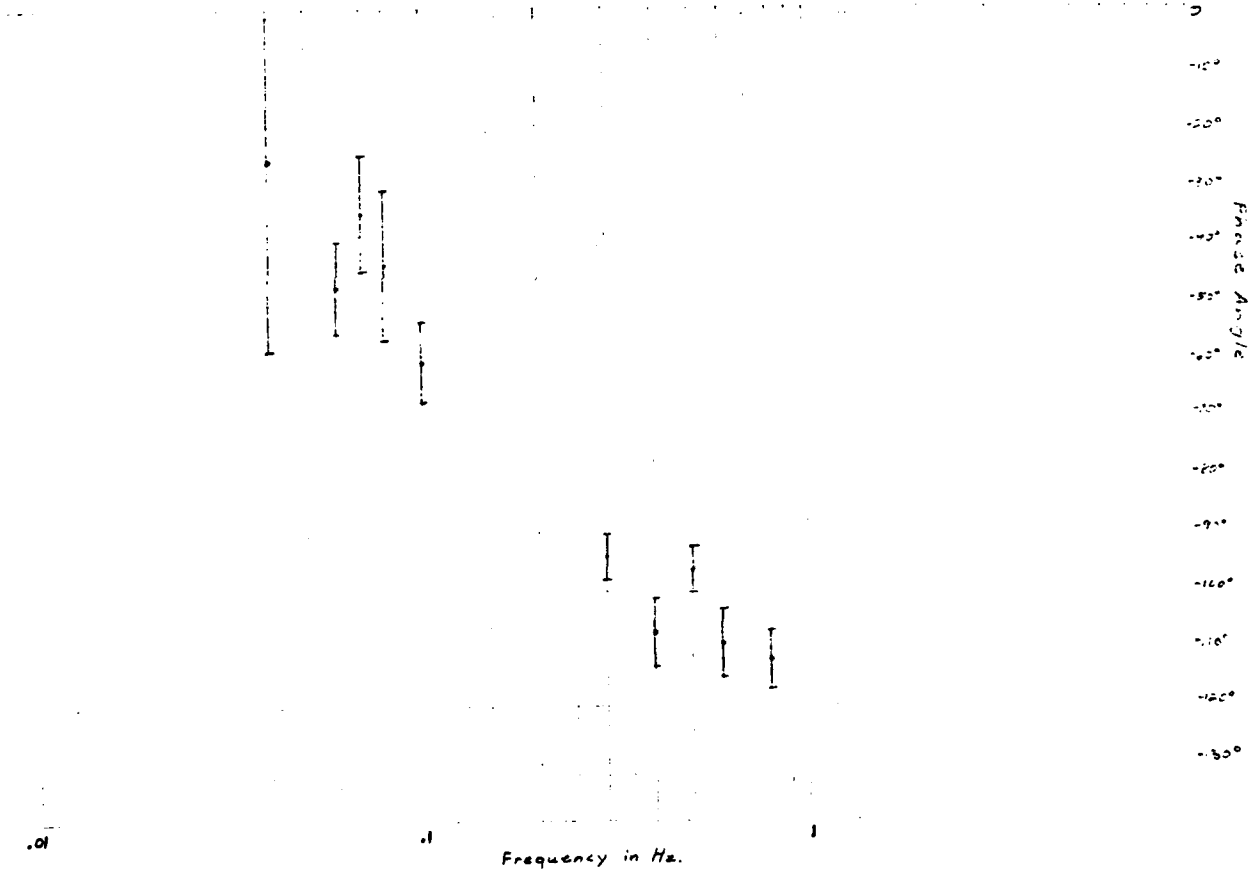


Figure 10. Phase Bode Plot of Mouse #12
Left eye, clockwise data

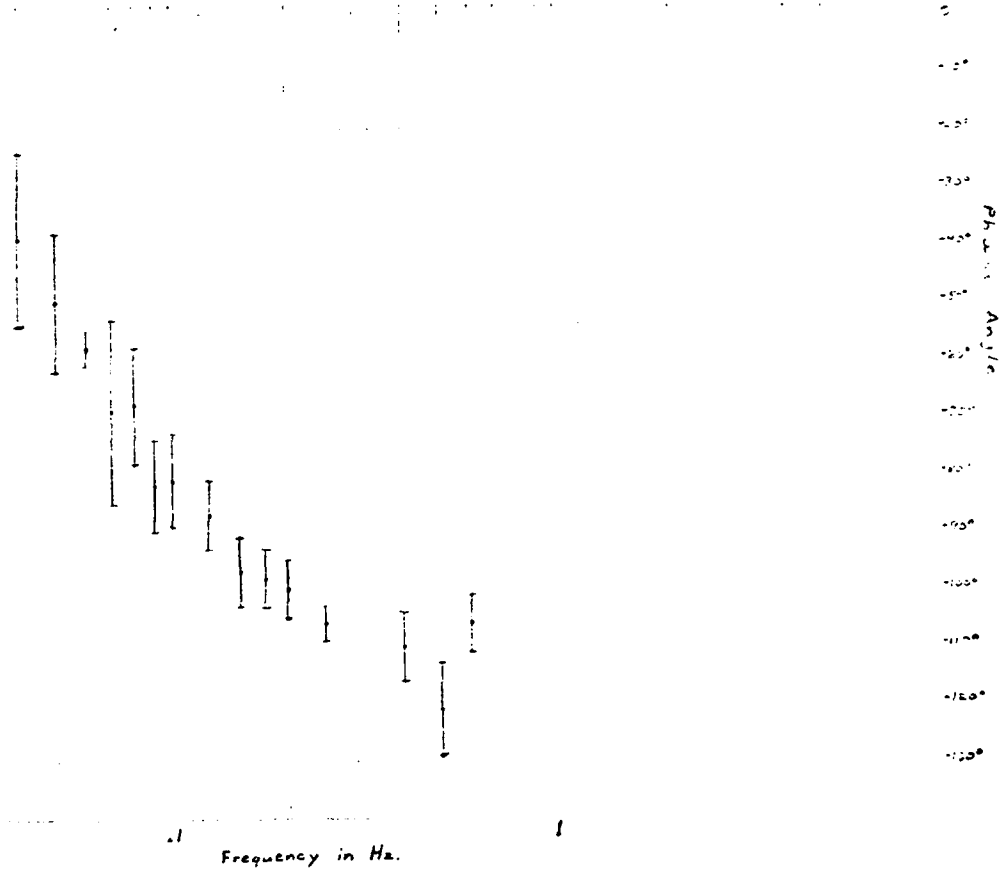


Figure 11. Phase Bode Plot of Mouse #12
Left eye, counterclockwise data

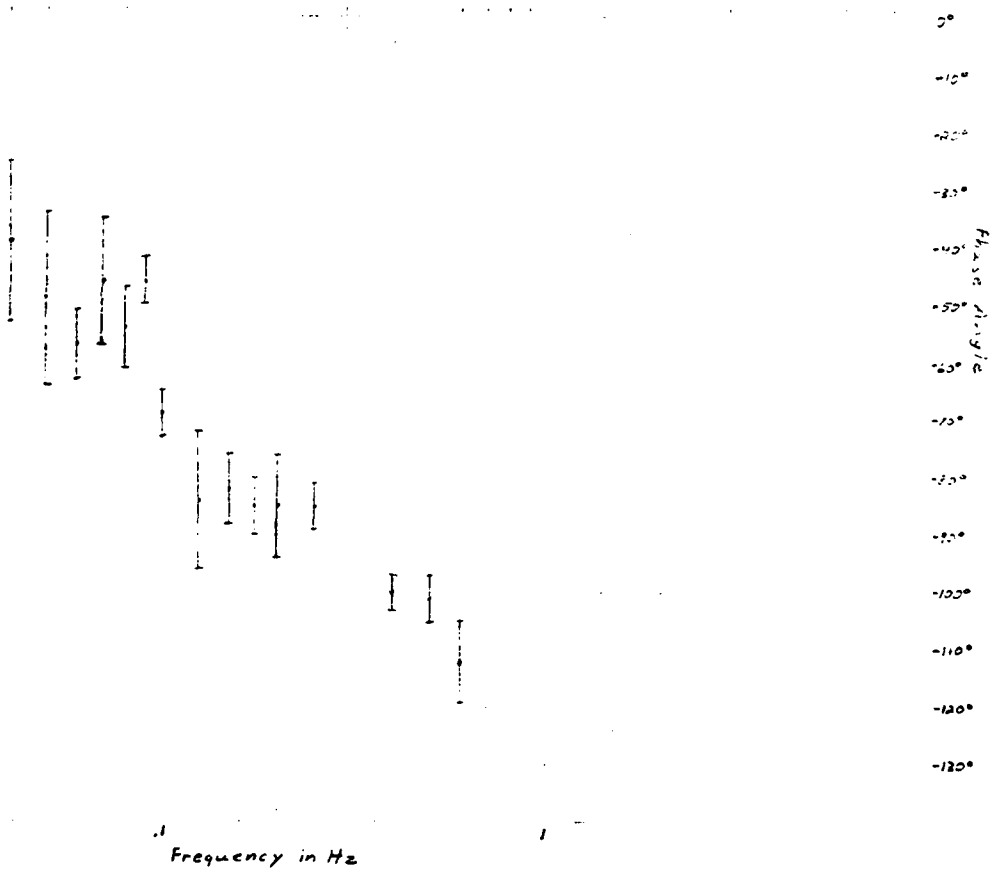


Figure 12. Phase Bode Plot of Mouse #4
Left eye, clockwise data

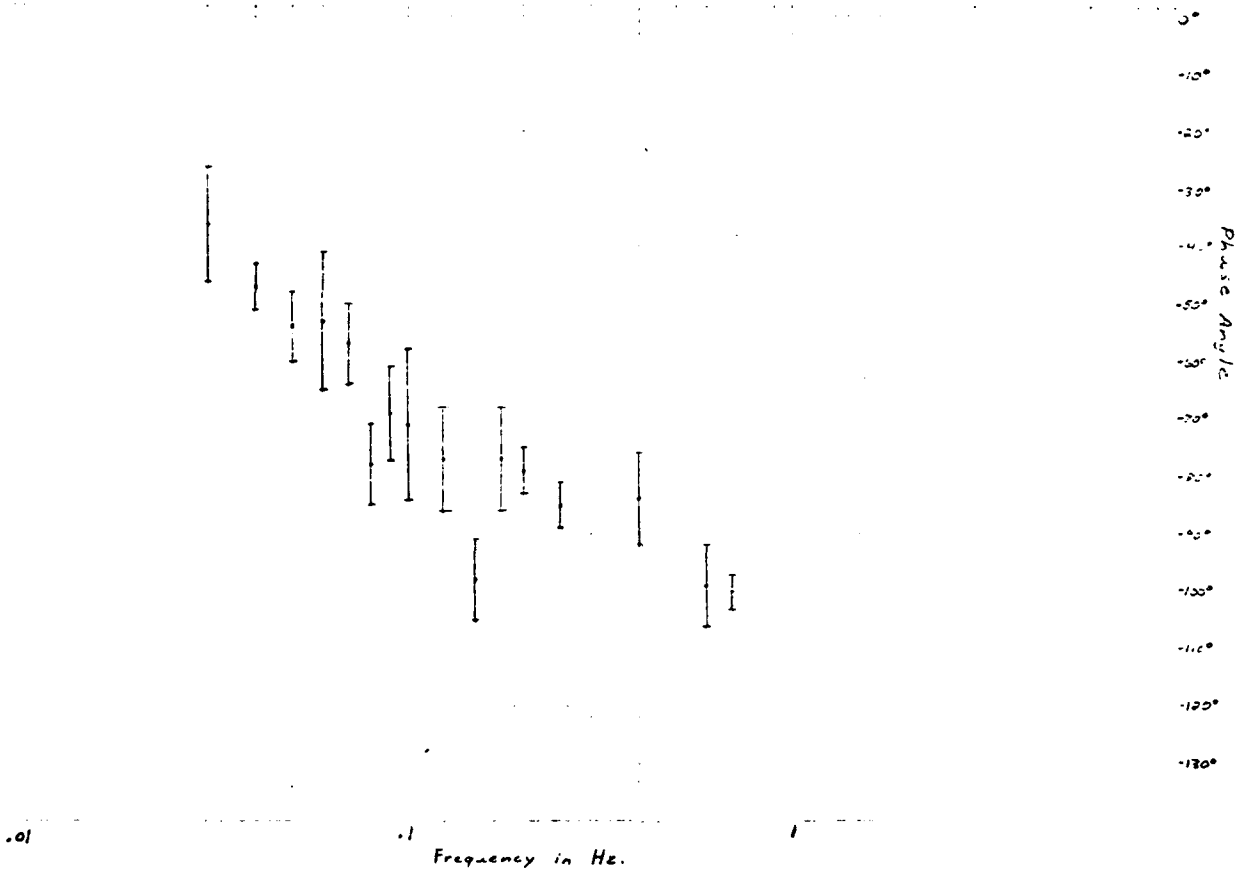


Figure 13. Phase Bode Plot of Mouse #4
Left eye, counterclockwise data

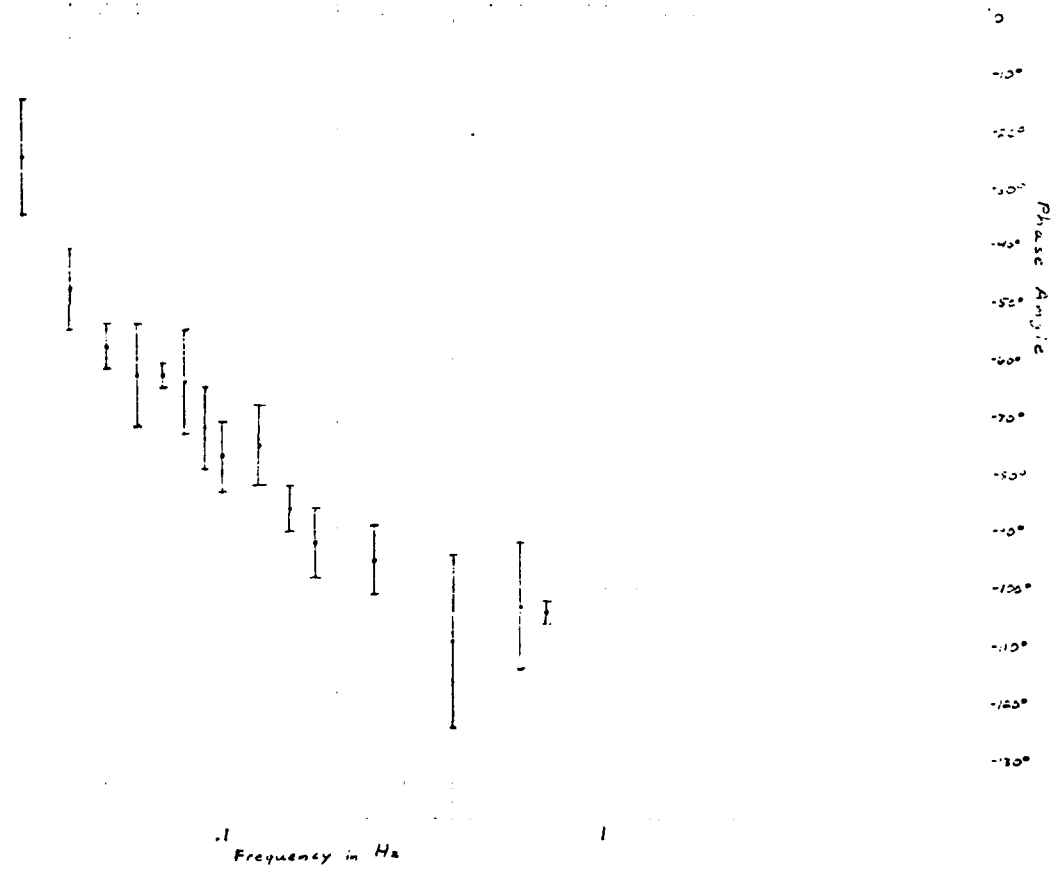


Figure 14. Phase Bode Plot of Mouse #13
Left eye, clockwise data

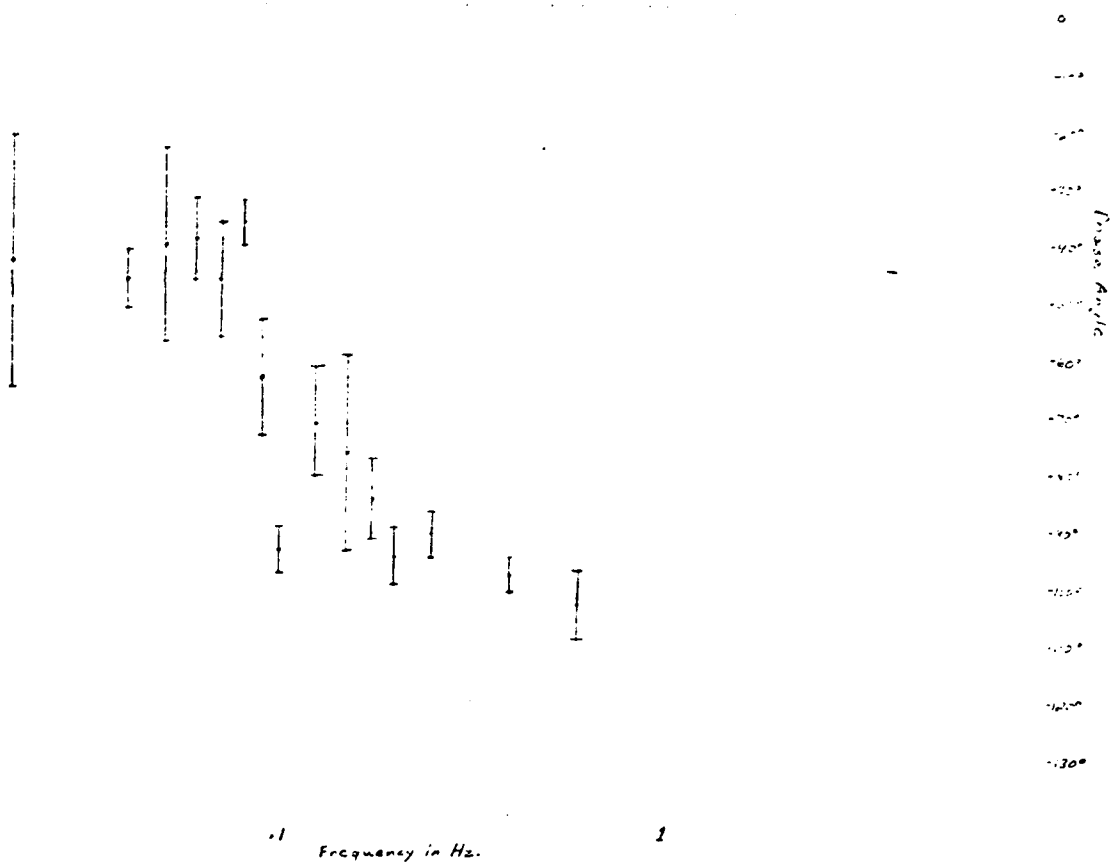


Figure 15. Phase Bode Plot of Mouse #13
Left eye, counterclockwise data

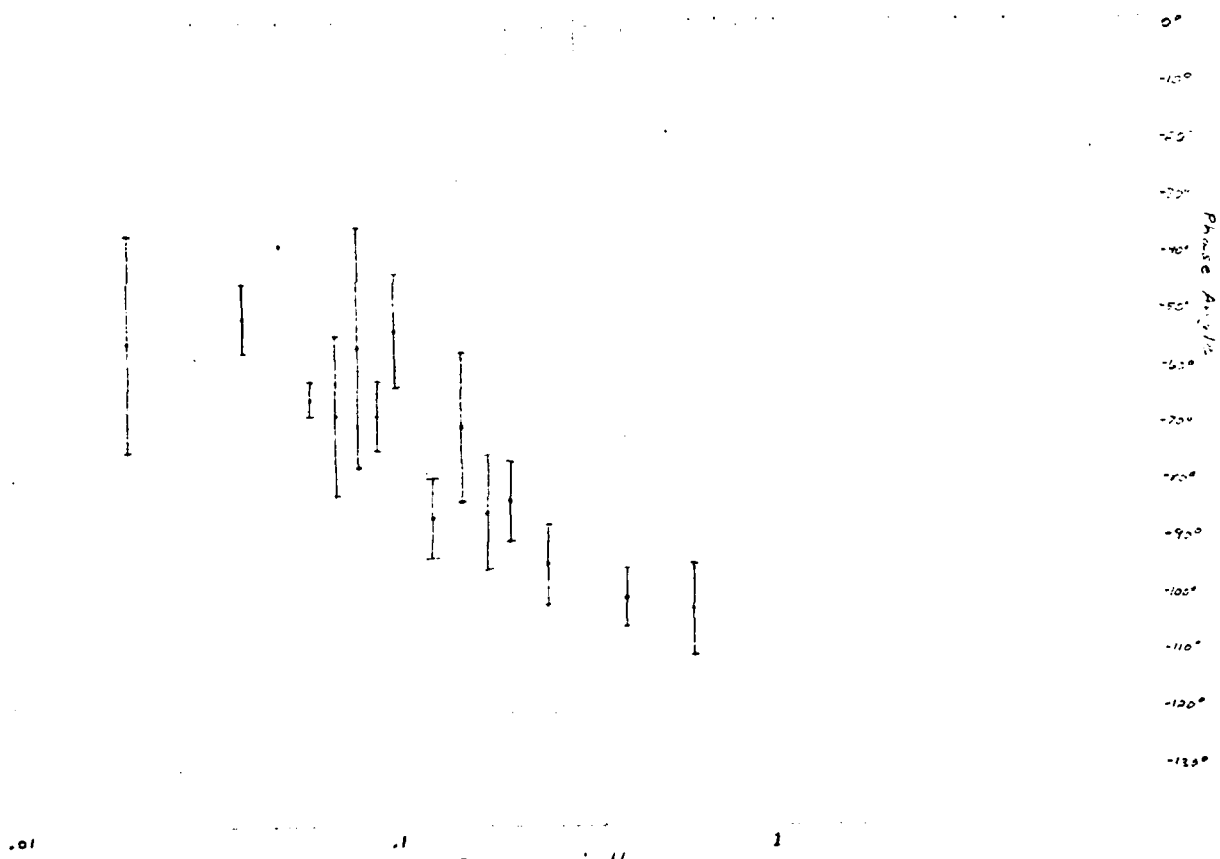


Figure 16. Phase Bode Plot of Mouse #19
Left eye, clockwise data

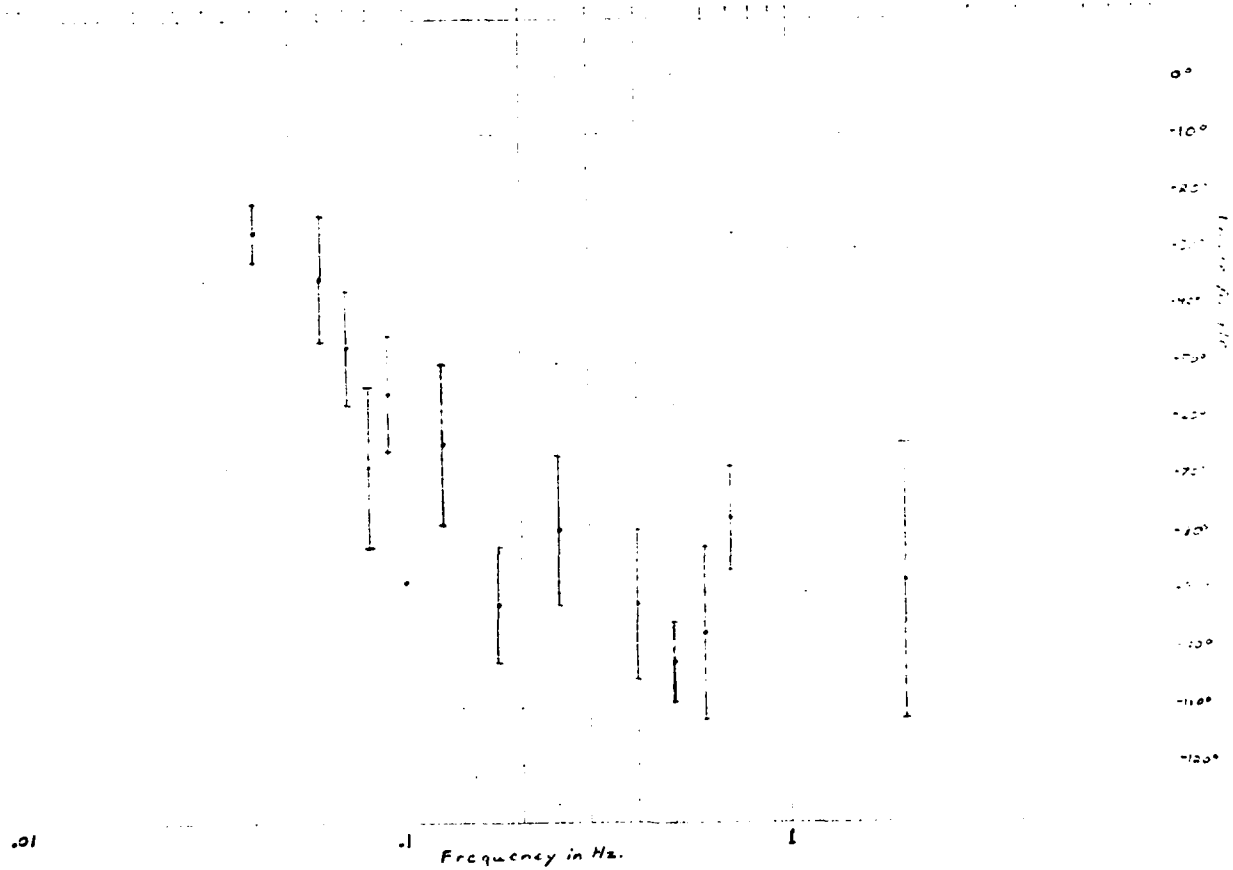


Figure 17. Phase Bode Plot of Mouse #19
Left eye, counterclockwise data

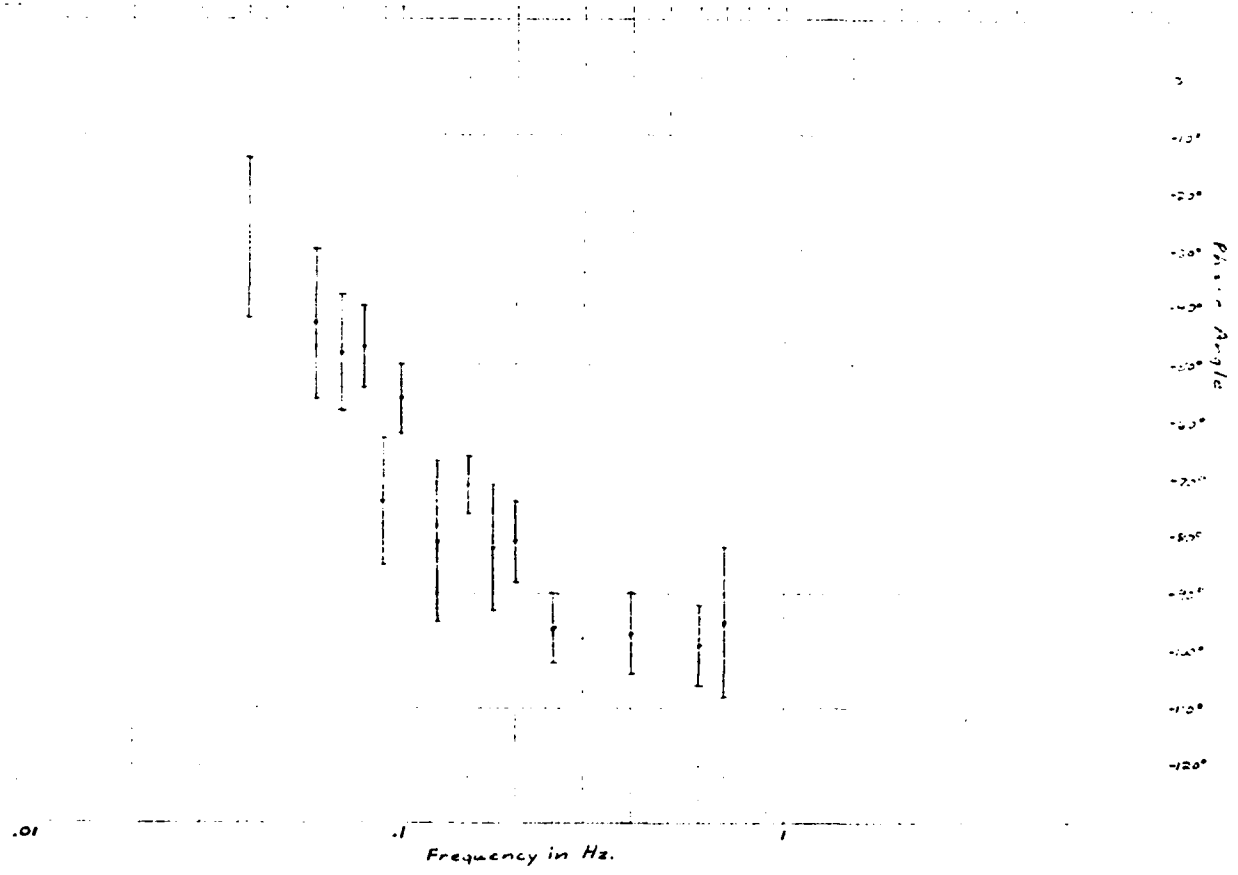
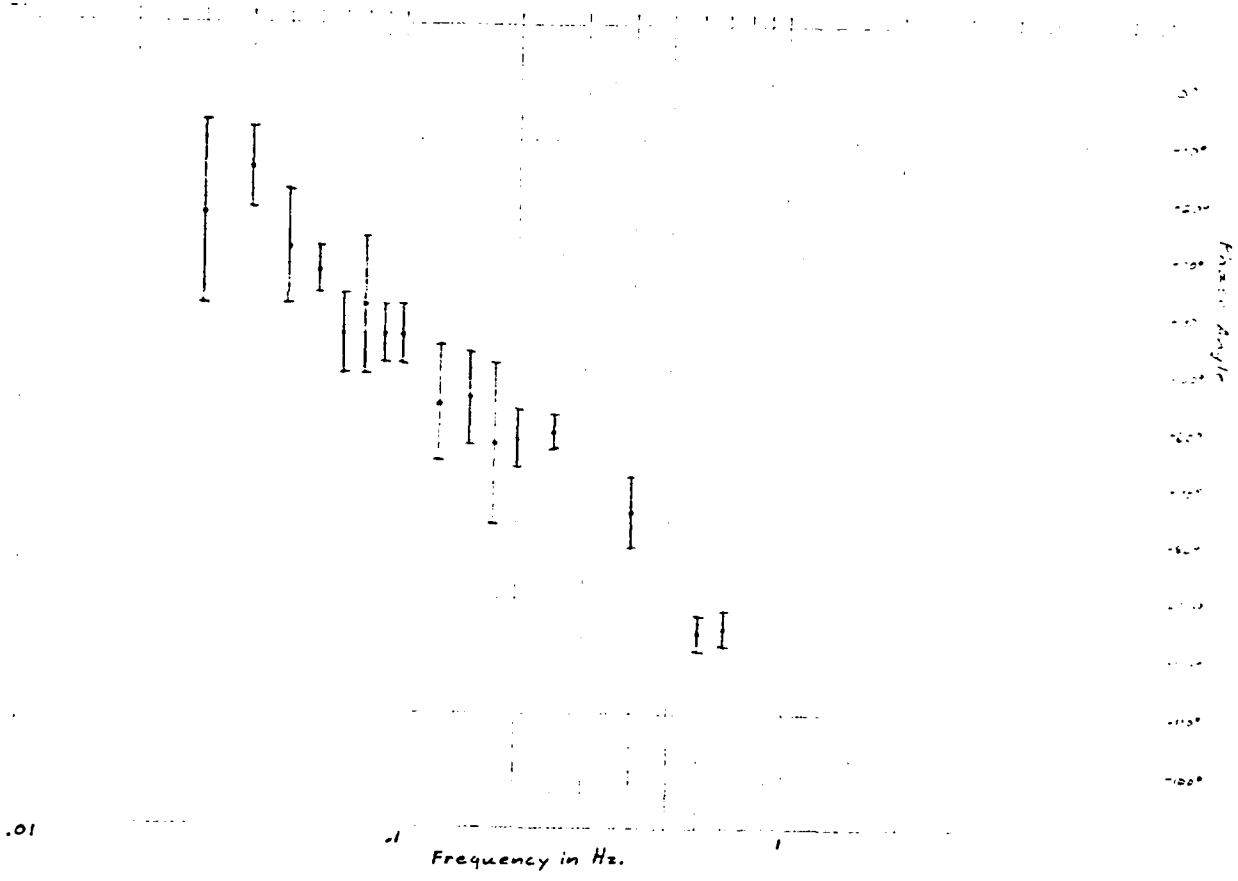


Figure 18. Phase Bode Plot of Mouse #18
Left eye, clockwise data



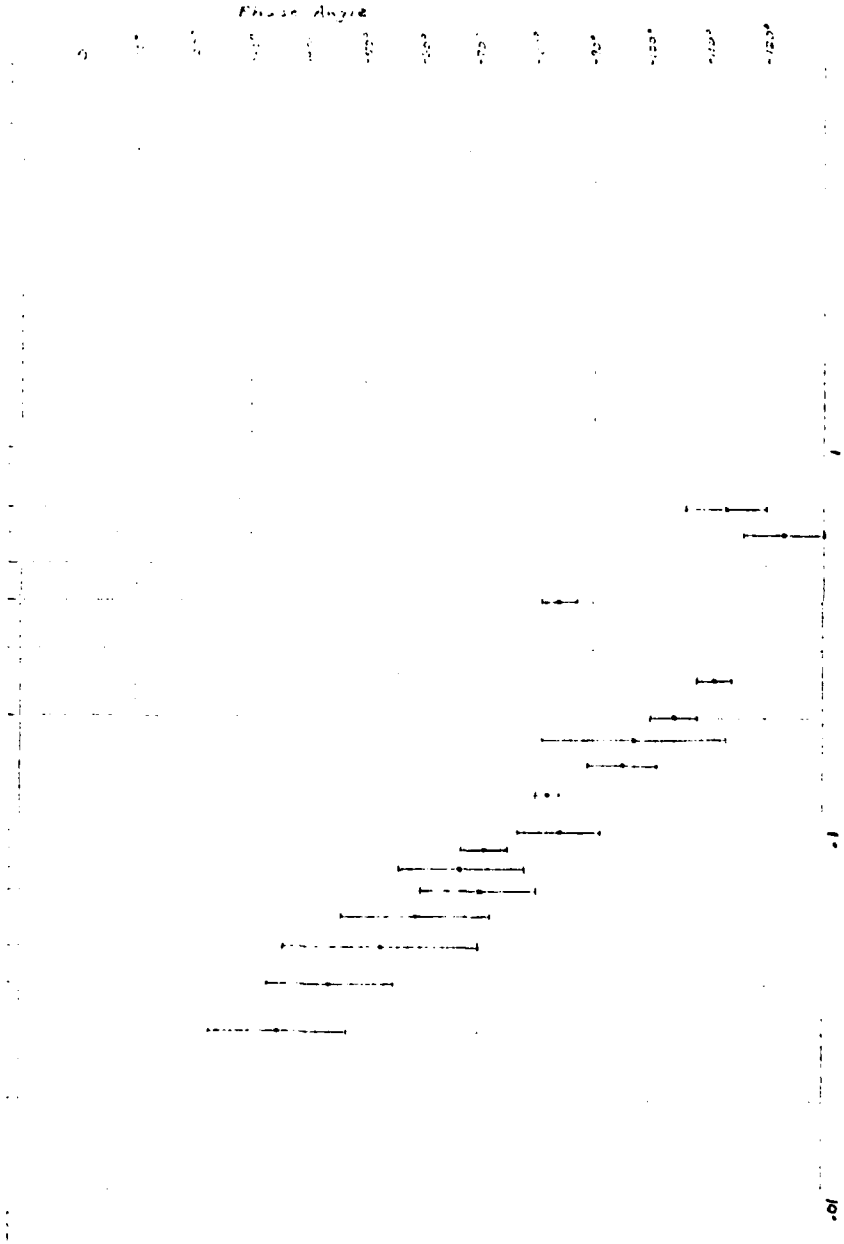


Figure 19. Phase Bode Plot of Mouse #18
Left eye, counterclockwise data

Figure 20. Phase Bode Plot of Mouse #3
Left eye, clockwise data

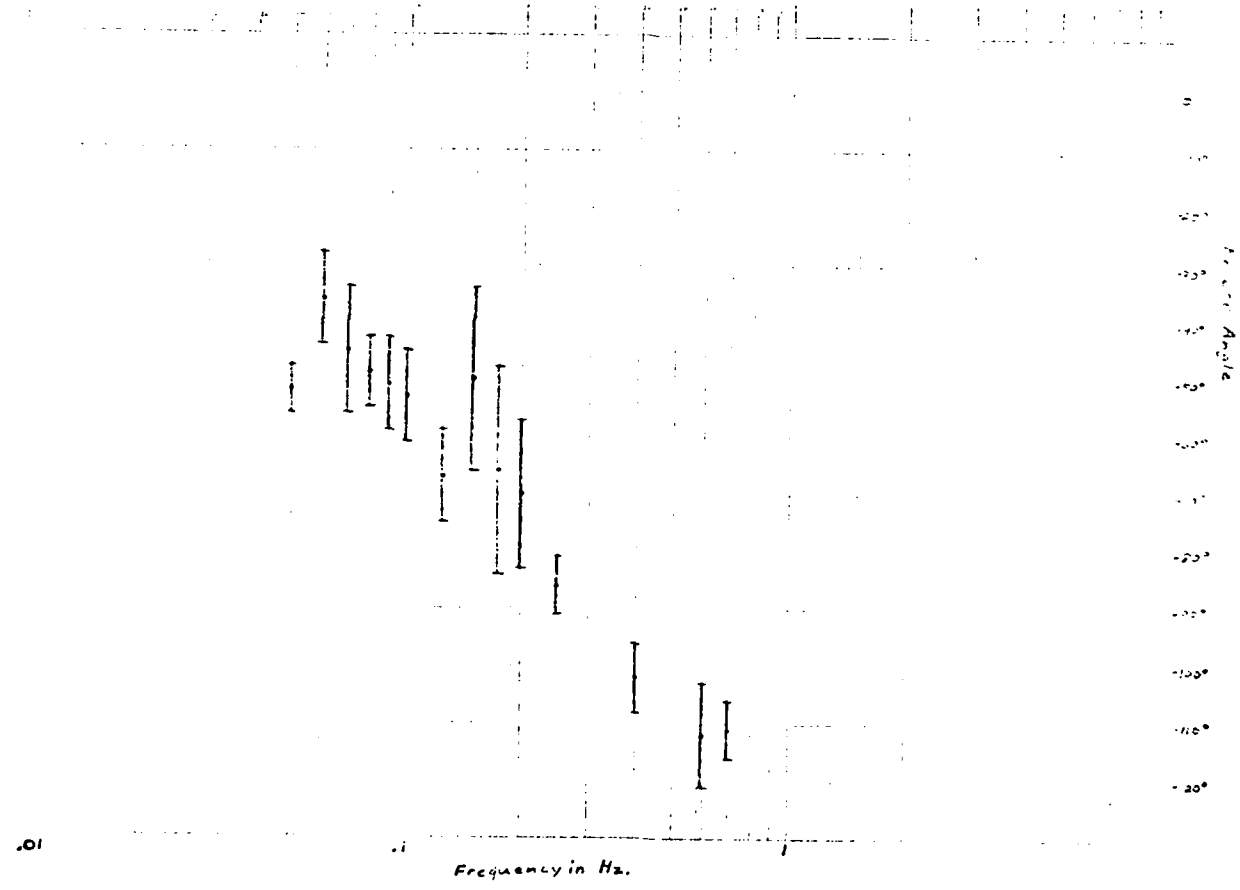


Figure 21. Phase Bode Plot of Mouse #3
Left eye, counterclockwise data

Figure 22. Phase Bode Plot of Mouse #11
Left eye, clockwise data

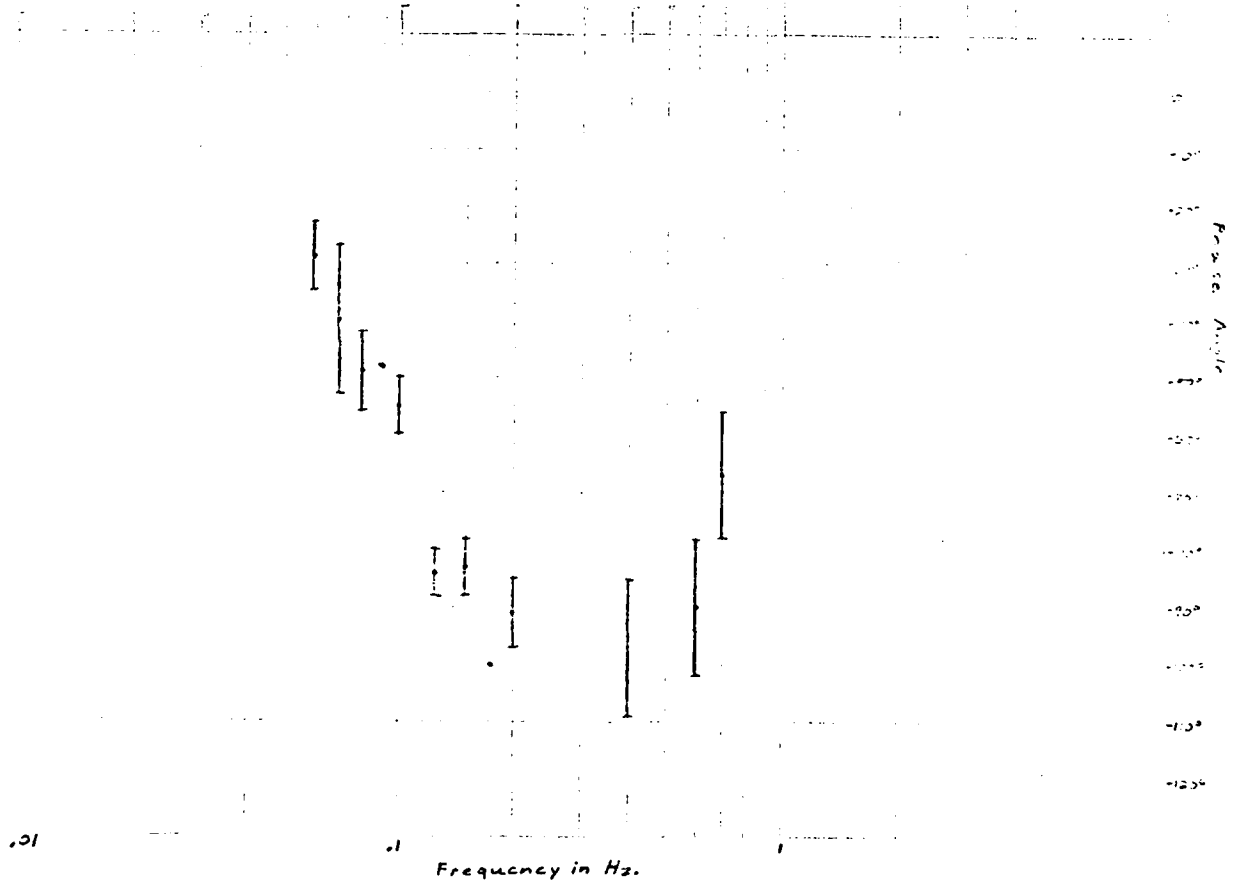
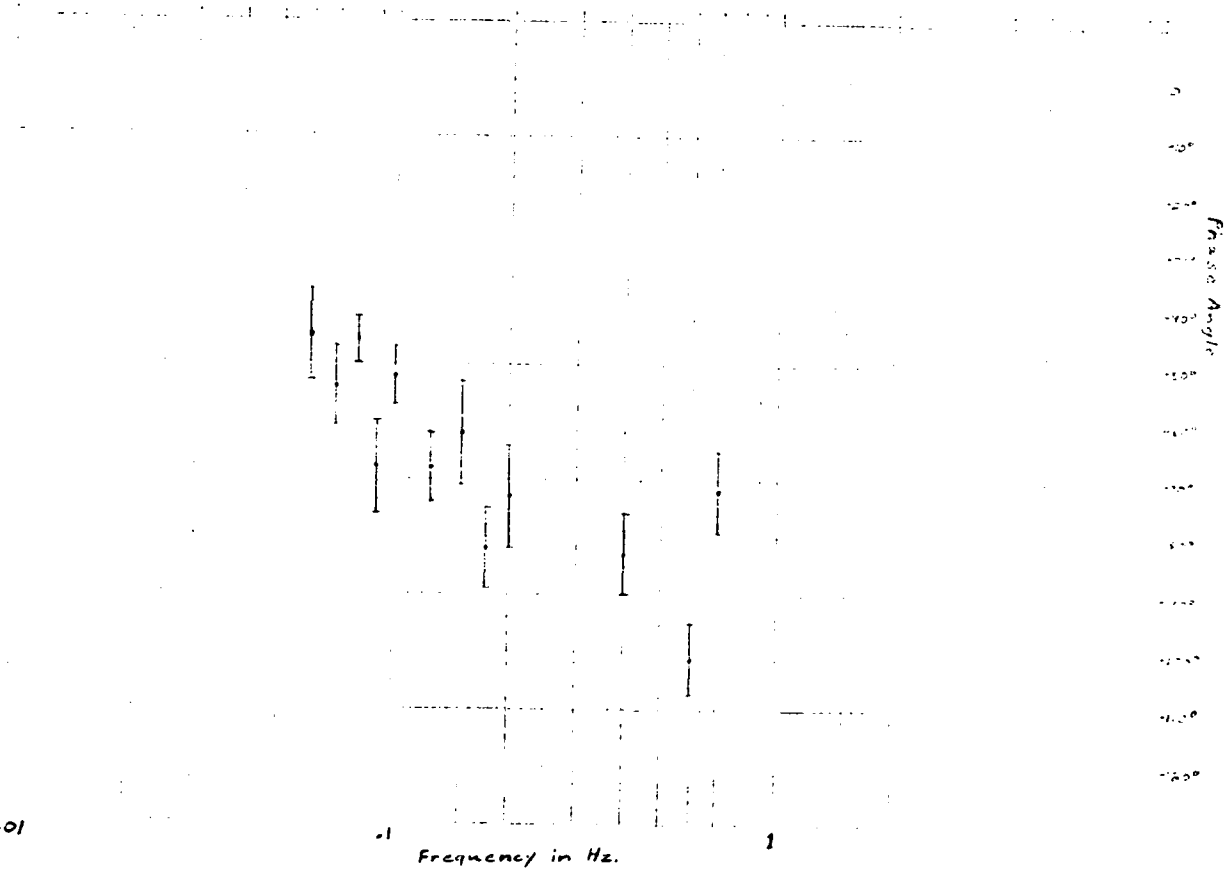


Figure 23. Phase Bode Plot of Mouse #11
Left eye, counterclockwise data



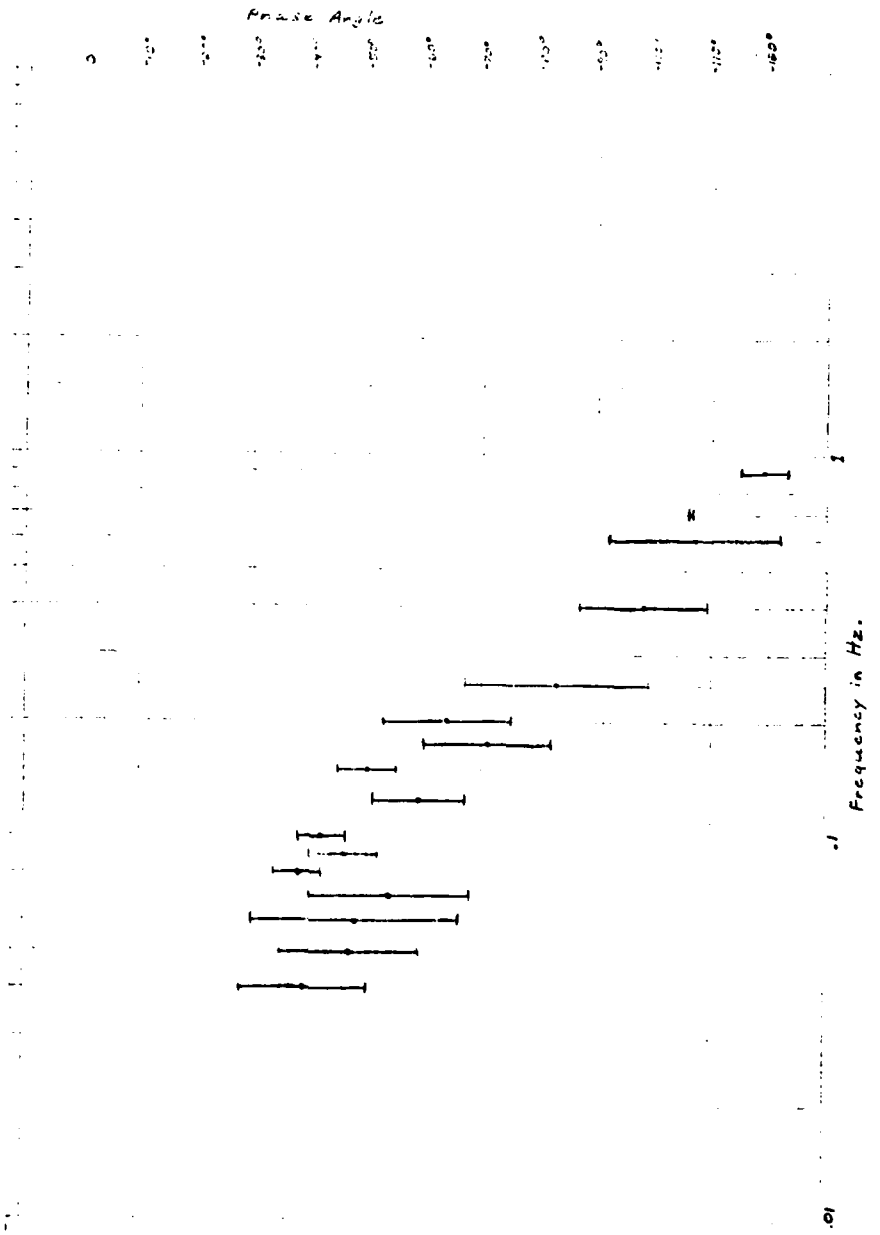


Figure 24. Phase Bode Plot of Mouse #17
Left eye, clockwise data

Figure 25. Phase Bode Plot of Mouse #17
Left eye, counterclockwise data

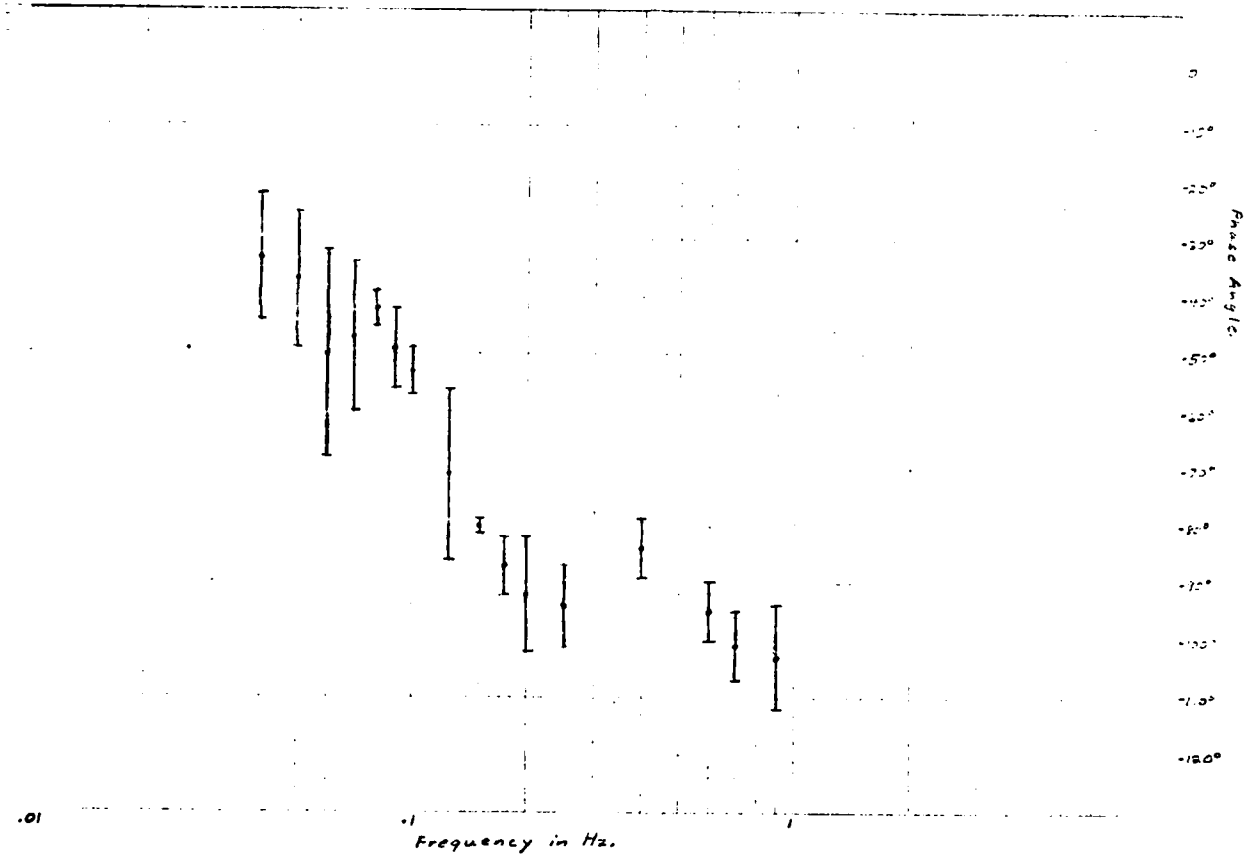


Table XI

Summary of Normal Swimmers - Left Eye

(Mice #'s 15, 10, 12, 4, 13, 18, and 19)

Clockwise Motion

Frequency in Hz	Mean Phase Angle in Degrees	Standard Deviation in Degrees
.03	-34	10
.04	-35	12
.05	-40	12
.06	-40	10
.07	-51	11
.08	-58	16
.09	-62	13
.1	-71	17
.125	-69	12
.15	-79	20
.175	-81	13
.2	-81	15
.25	-83	15
.3	-95	8
.4	-94	13
.5	-103	16
.6	99	5
.7	-92	10
.8	-112	--
1.0	-101	--

Table XI (Cont.)

Counterclockwise Motion

Frequency in Hz	Mean Phase Angle in Degrees	Standard Deviation in Degrees
.03	-30	7
.04	-39	11
.05	-45	12
.06	-56	9
.07	-57	14
.08	-55	9
.09	-64	11
.1	-70	10
.125	-80	6
.15	-80	10
.175	-90	7
.2	-92	13
.25	-97	8
.3	-96	2
.4	-100	9
.5	-107	8
.6	-108	7
.7	-105	8
.8	-112	--
1.0	-104	--

Overall average standard deviation = 9.8°

Table XII

Summary of Underwater Circular Swimmers - Left Eye

(Mice #'s 3, 17 and 11)

Clockwise Motion

Frequency in Hz	Mean Phase Angle in Degrees	Standard Deviation in Degrees
.04	-39	--
.05	-50	4
.06	-38	10
.07	-46	7
.08	-45	6
.09	-48	3
.1	-50	7
.125	-70	13
.15	-61	19
.175	-79	18
.2	-75	14
.25	-84	2
.4	-99	3
.6	-103	12
.7	-95	24
.9	-119	--

Counterclockwise Motion

.04	-33	--
.05	-34	4
.06	-45	6
.07	-48	5
.08	-48	8
.09	-56	11
.1	-56	7
.125	-69	2
.15	-73	9
.175	-81	6
.2	-85	10
.25	-90	5
.4	-88	4
.6	-97	3
.7	-90	16
.9	-103	--

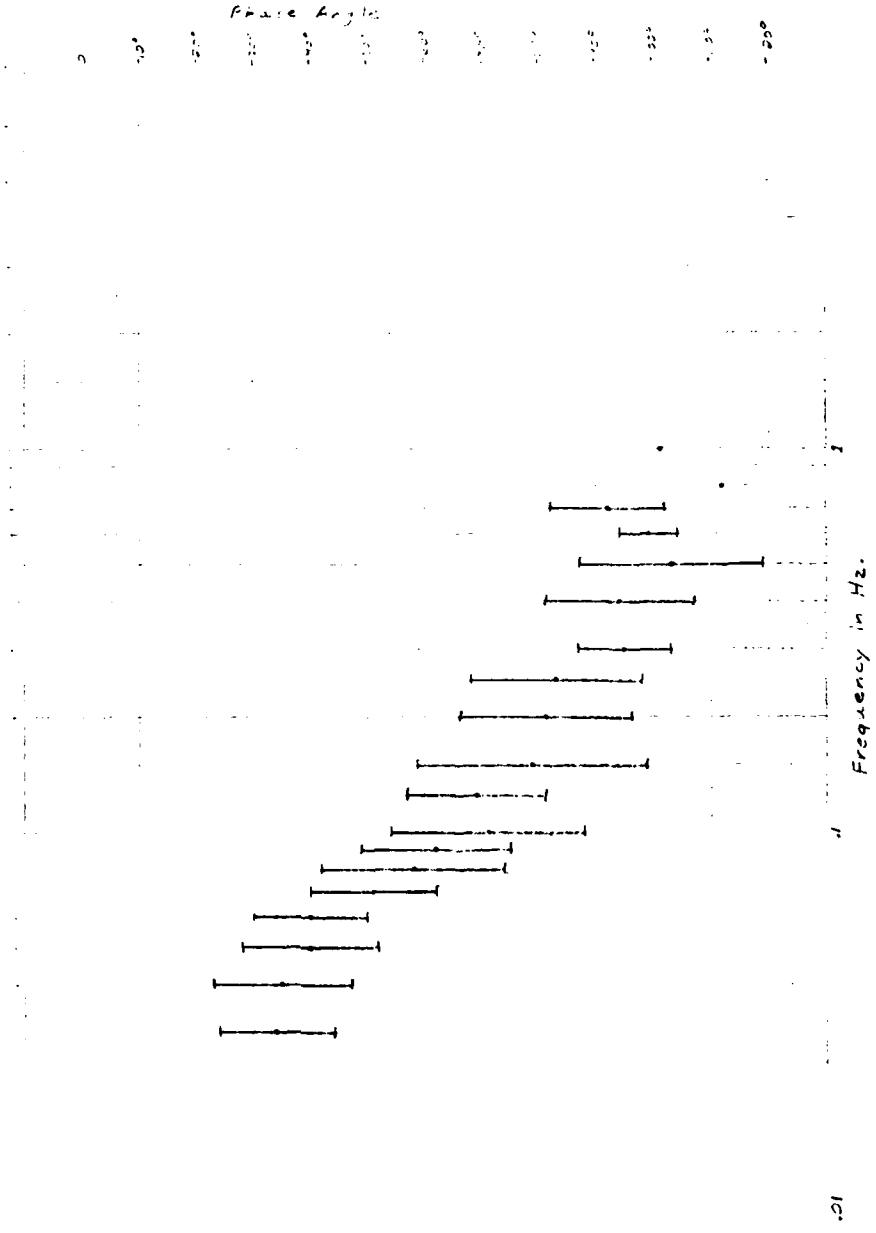
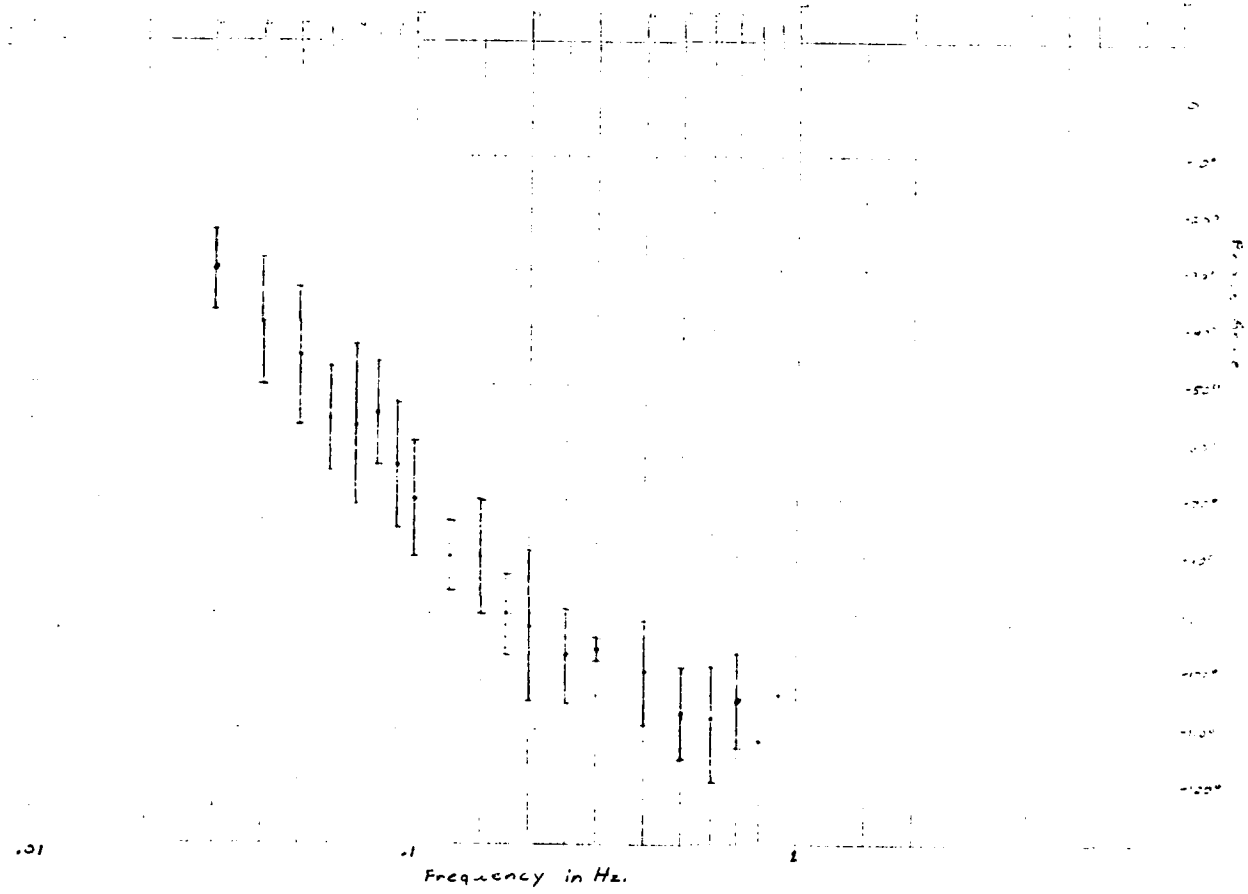


Figure 26. Phase Bode Plot of Combined Normal Swimming Mice - Clockwise Data

Figure 27. Phase Bode Plot of Combined Normal Swimming Mice - Counterclockwise Data



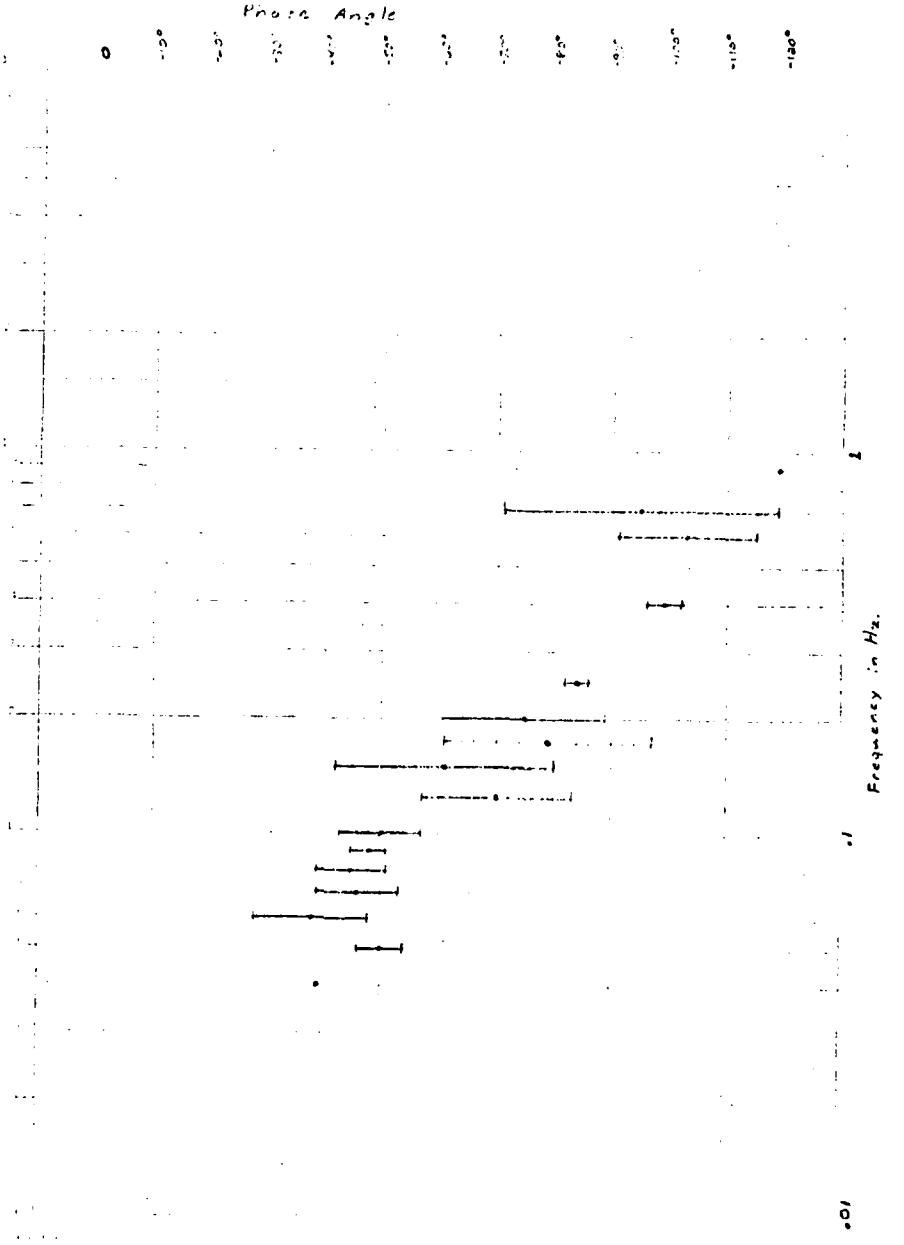


Figure 28. Phase Bode Plot of Combined Underwater Circular Swimmers - Clockwise Data

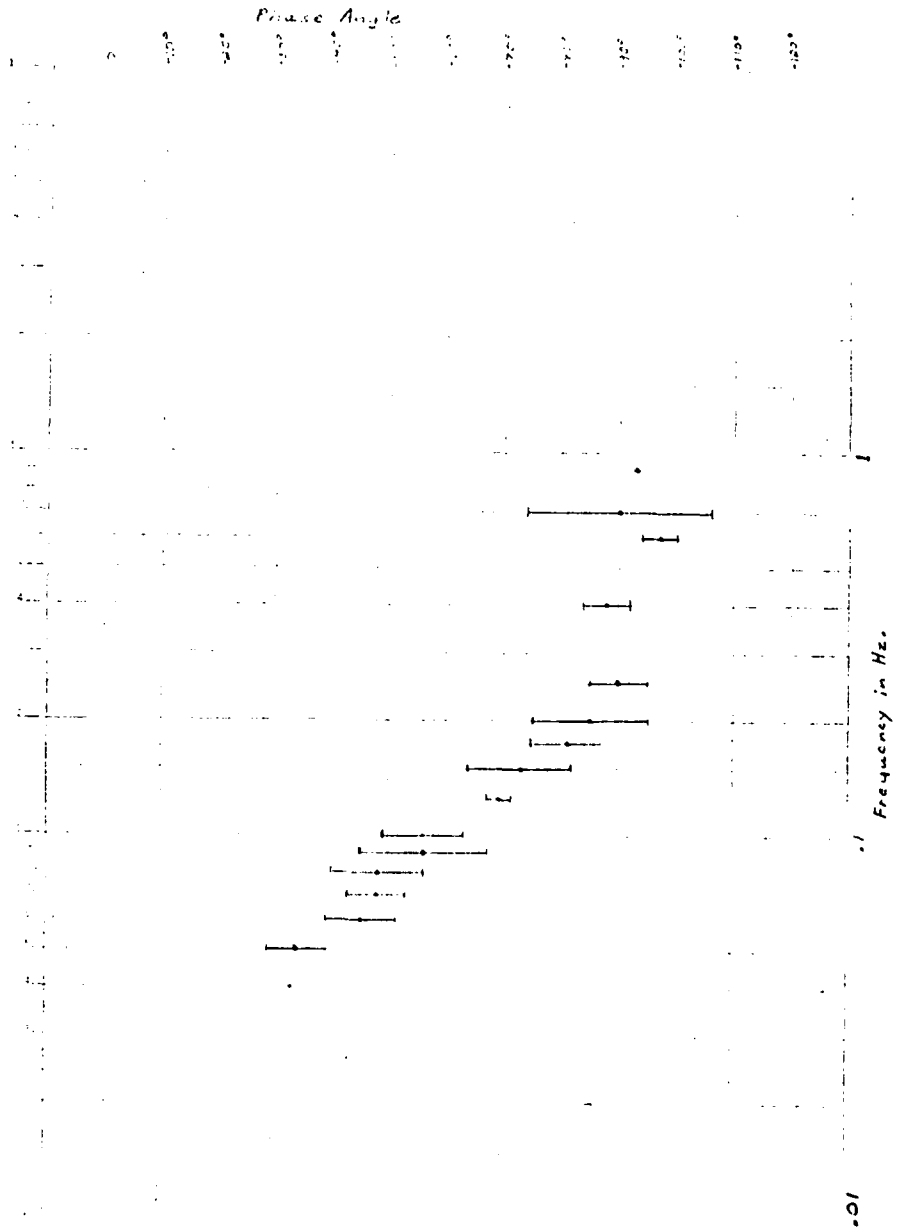


Figure 29. Phase Bode Plot of Combined Underwater Circular Swimmers - Counterclockwise Data

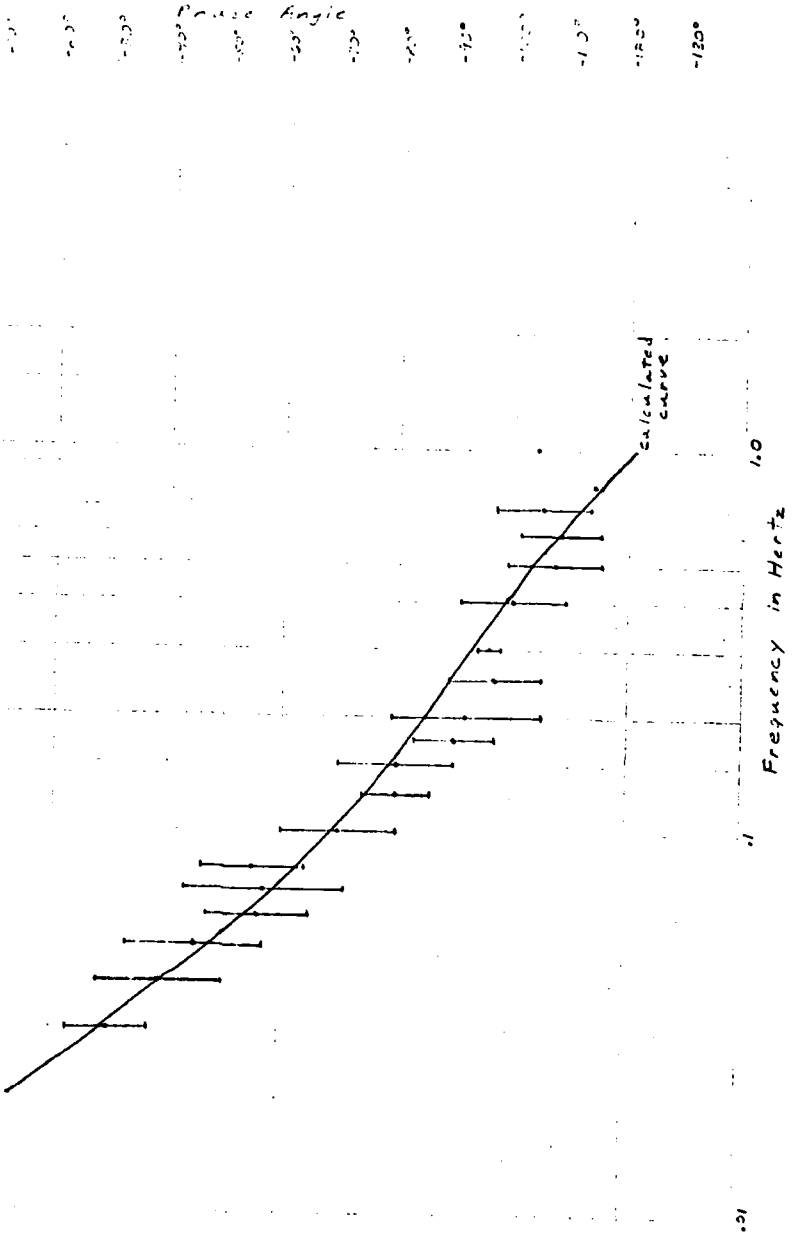


Figure 30. Computed Phase Bode Plot for Normal Swimmers Overlayed on Counterclockwise Data for Normal Swimmers. (Corner Frequencies for Computed Plot are .005, .04 and 1.25 Hz.)

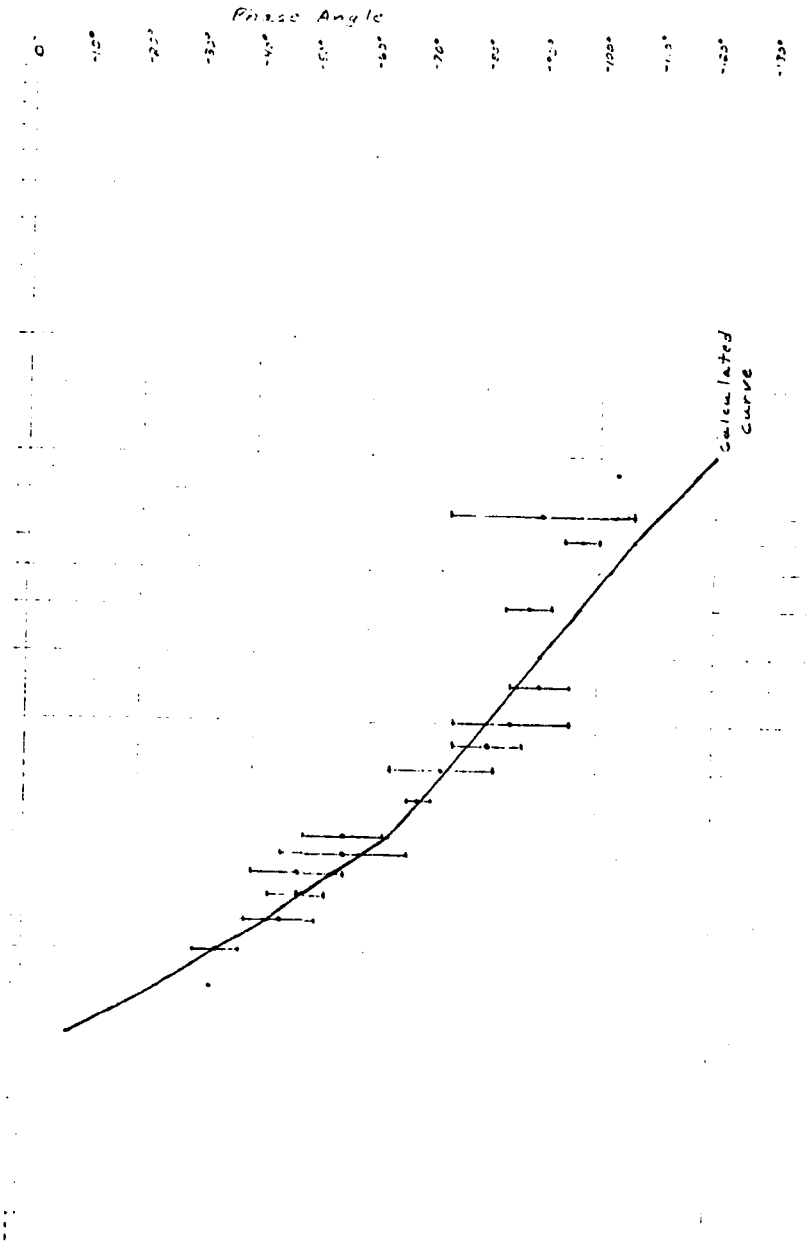


Figure 31. Computed Phase Bode Plot for Underwater Circular Swimmers Overlayed on Counterclockwise Data for Underwater Circular Swimmers. (Corner Frequencies for Computed Plot are .017, .04 and 1.25 Hz.)

REFERENCES

1. Coccia, M.R., The influence of the otoliths on semicircular canal induced nystagmus. Ph.D. Dissertation. Columbus, Ohio: The Ohio State University, 1975.

2. Groen, J.J., The semicircular canal system of the organs of equilibrium - I. Physics in Medicine and Biology, 1: 103-117, 1956-1957.

3. Hixson, W.C., Frequency response of the oculovestibular system during yaw oscillation. NAMRL-1212. Pensacola, Florida: Naval Aerospace Medical Institute, 1974.

4. Jones, G.M., Nystagmography - A useful tool in basic and applied investigations. In: The Use of Nystagmography in Aviation Medicine. AGARD-DP-128. Pensacola, Florida, 1973, pp. A12-1 to A12-13.

5. Lansberg, M.P., The modulating influence of the otolith organs on semicircular canal functions. In: The Role of the Vestibular Organs in the Exploration of Space. NASA SP-77. Washington, D.C.: U.S. Government Printing Office, 1965, pp. 69-76.

6. Malcolm, R. and Melvill-Jones, G., A quantitative study of vestibular adaptation in humans. Acta Otolaryng. (Stockh.), 70: 126-135, 1970.

7. Precht, W., Vestibular mechanisms. Annual Review of Neuroscience, 2: 265-289, 1979.

8. Stockwell, C.W., and Collins, W.E., Practical problems in clinical nystagmography II Sources of Error. In: The Use of Nystagmography in Aviation Medicine. AGARD-DP-128. Pensacola, Florida, 1973, pp. A3-1 to A3-10.

9. Young, L.R., and Oman, C.M., Model for vestibular adaptation to horizontal rotation. Aerospace Medicine, 40: 1076-1080, 1969.